

**The
Development and Testing
of an
Artificial Anal Sphincter**

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Very lame and imperfect theories are sufficient to suggest useful experiments which serve to correct these theories and give birth to others more perfect. These, then, occasion further experiments which bring us still nearer to the truth; and in this method of approximation we must be content to proceed, and we ought to think ourselves happy if, in this slow method, we make any real progress.

Joseph Priestly (1733-1804)

To my daughters Danai and Maria,

my wife Evangelia,

my mother Nedi and

my grandmother Danai.

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ABSTRACT

The physiological mechanisms for achieving faecal continence and the results of the surgical methods to correct incontinence are reviewed. The devices hitherto designed to attempt to achieve continence artificially are discussed and an analysis of 4130 reported complications of a successful device for the control of urinary incontinence (the AMS 800) are presented. Based on these reviews, the need to design and evaluate a prosthetic anal sphincter is identified and such a device is presented in this thesis.

The effect of circumferential occlusive pressure on the blood flow of porcine colon was assessed by a Laser Doppler flow meter. It was demonstrated that distal blood flow is reduced by 50% at 52 mmHg. The occlusion pressure required to achieve continence to semi-solids was shown to be reduced by the introduction of angulation both in a theoretical model and experimentally, using a specifically designed faecal substitute.

The Neosphincter was, therefore, designed to simulate the normal physiology of the anorectum by closing and angulating the bowel without causing crenation and ischaemia.

The design parameters of the device were evaluated in an *in-vitro* model and its placement assessed in a series of acute animal experiments in a porcine model. The effects of the prosthesis set at an operating occlusion pressure of 33-45 mmHg were then evaluated in survival animal experiments by implantation in Yucatan minipigs for up to 20 weeks. The device produced faecal continence in 85% of the activation times without causing ischaemic injury. Mechanical complications associated with the control pump were encountered and design faults were identified. A new pump was designed by the author.

The effect of Neosphincter function on blood flow distribution in the human colon was studied during colectomy using a prototype Laser Doppler flow scanner. Blood flow remained greater than 50% at 60 mmHg occlusion pressure.

The data presented show that the Neosphincter achieves continence in the mini-pig model and further suggest that continence would be achieved in the human without producing intestinal ischaemia. Ethical approval has been obtained to proceed to trials in human patients.

STATEMENT OF AUTHOR

I declare that during the course of this study, all the practical work was performed by me, with the exceptions listed in the acknowledgments section. In general the overall planning, experiments (*in-vitro* and *in-vivo*), assessment and analysis were performed by myself, but much of the daily routine gathering of data was performed by veterinary nursing staff. The acute animal experiments were supported by a Grant from the Scottish Office Home and Health Department (Ref. No.: R/NMD/2/2/C371) and further support for the survival experiments was received through another Grant from the same source (Ref. No.: K/MRS/50/C1841). The experimental and investigative protocol of the survival experiments was designed by myself and I also performed all experimental techniques. The pressure parameter recordings were taken by Mr K.B. Carter and the routine histological sections were performed by Dr I. McCandleish. All sections were also examined and analyzed by myself. I also confirm that neither this work nor any part of it has been submitted for another degree to this or any other University.

14th August 1996.

PREFACE

The work presented in this thesis was undertaken in the following Establishments:

Wellcome Institute for Surgical Research -All animal experiments.

Department of Coloproctology and University Department of Surgery, Royal Infirmary, Glasgow

-*In-vitro* sphincter evaluation
-*In-vitro* engineering studies
-Laser Doppler Human studies.

Department of Clinical Physics and Bioengineering, University of Glasgow

-*In-vitro* engineering studies.

Department of Pædiatric Surgery, Royal Hospital for Sick Children, Yorkhill, Glasgow

-Design and assembly of prototype
automatic control devices.

Explanation of the Literature quoted

The papers quoted are those in English unless they were important works and were, therefore, translated. Copies of all the original Patent Submissions of Artificial Sphincter Devices were obtained through a commercial Patent Agent and reviewed. This thesis was commenced in 1995 and as a general policy, literature up to that point is included in the introductions of the appropriate chapters. Relevant important papers appearing later are included in the discussion.

Reference lists appear at the end of each chapter in the order that they appear in the text. A complete list of references indexed alphabetically appears at the end of the thesis.

Ethical considerations

All animal experiments were performed under the Project License No. PPL 60/01371 and the Authors' Personal Licenses, in accordance with the Animals (Scientific Procedures) Act (1986) and the relevant Home Office Rules and Regulations.

Informed consent was obtained from all patients involved in the Laser blood flow study.

Skills and disciplines acquired during the period of study for this Thesis

My previous experience in medical scientific methods and research and handling of experimental animals which was developed during the intercalated year of my undergraduate studies in Edinburgh University and the subsequent years of my practice, in electronics and engineering, along with my surgical experience proved invaluable for the execution of the current task.

My computer literacy was developed during the period of study for this Thesis and has progressed from being a daunting undertaking to becoming an invaluable tool. Apart from the basic techniques (word processing, file managing etc.), I learned basic and advanced drawing techniques and computer aided design (CAD) drawing. I drew all illustrations that were not reproduced from other sources personally, the only exception being the engineering drawings of the original pump prototype and the evolution design. The former were hand drawn by Mr W. Richardson and the latter by Mr P. Agius. I became fluent in scientific data analysis, graphing and presentation methods and mathematical curve fitting transforms. The statistical analysis of the data was helped by the course on medical statistics (University of Glasgow) that I attended. I also designed and constructed the databases required to analyze the data.

The following computer programs were used:

- Word for Windows v6.0
- Excel v5.0
- Access v2.0
- Sigma Plot v1.02
- Key CAD v2.0
- Corel Draw v4
- MS Draw
- Minitab v9
- Laser Scan analysis software (Essex & Byrne[©])
- PZP for DOS image capture software v2

It was also necessary to develop knowledge of rheological principles and this was achieved by private study and with the help of Professor James Ferguson and Dr Nick Hudson from the Department of Pure and Applied Chemistry, University of Strathclyde.

This Thesis was started upon completion of a year of intensive research while on secondment from the Department of Pædiatric Surgery and written during a very busy Clinical post without secretarial input. The amount of discipline required from myself I chose to accept, and for a similar if not much greater amount of discipline, understanding and help shown by my wife I am truly grateful.

ACKNOWLEDGMENTS

Firstly, I would like to thank Professor D.G. Young and Mr I.G. Finlay, who have been a constant source of support, encouragement, guidance and helpful criticism during the preparation of this manuscript and Mr D.C.C. Bartolo, Department of Surgery, Royal Infirmary, Edinburgh who has kindly supervised my Candidature.

Furthermore I express my wholehearted indebtedness to my Teachers: The Late Vahan Bedelian, Reverend Father Adamantios Kykkotis, Professor W.E. Watson, Mr I.B. MacLeod, Mr W.H. Bissett, Mr I.K. Drainer, Mr A.H.B. Fyfe and Professor D.G. Young who have, chronologically, shaped my character, guided me with their uncompromising principles, instructed me on Scientific Methods and supervised my apprenticeship in Surgical Technique.

Thanks also to:

Mr Ken Carter, Medical Physicist, for his painstaking preliminary work on the manufacture of the device, for performing the bulk of the pressure measurements and for his general ability to "make things happen", even with dated electronic equipment.

Mr Robert Wright, Senior Chief MLSO, for his expert surgical assistance, constant advice on equipment, software and hardware, presentation preparation and tuition in the "Scottish Culture".

Dr Donald MacMillan, for critical appraisal of results and methodology and for strengthening my computing foundations.

Mr Ken Greer for operating the Laser Doppler flow scanner during the human experiments.

Drs Joyce Ferguson, Jean Wilson, Michael Wilkinson and the staff at the Wellcome Surgical Institute for Veterinary advice and assistance during the long Operating and Radiology sessions and Dr Irene McCandleish for performing the Histological sections.

Ms Allison Stevenson at the Library of the Royal College of Surgeons of Edinburgh and the staff at the Glasgow Royal Infirmary and University Libraries for their help in locating many obscure references.

I have drawn upon the skills of numerous individuals and this list can by no means be exhaustive. There is a multitude of other people who, both knowingly and unknowingly, have contributed to this work through discussions, support or understanding to whom I wish to extend my most sincere thanks.

Presentations, Publications and Awards arising from this Thesis

Presentations

1. The development and testing of an artificial anal sphincter.

C.A. Hajivassiliou, K.B. Carter, W. Richardson, I.G. Finlay,
Royal Society of Medicine, London, January 1994.

2. The development and testing of an artificial anal sphincter:
Preliminary Implantation Results.

C.A. Hajivassiliou, K.B. Carter, W. Richardson, I.G. Finlay,
Caledonian Society of Gastroenterology, Edinburgh, February 1994.

3. A hydraulically operated artificial anal sphincter prosthesis.

C.A. Hajivassiliou, K.B. Carter, I.G. Finlay,
American Society of Colon and Rectal Surgeons 93rd Annual Congress,
Orlando, Florida, May 1994.

4. Achieving continence artificially.

C.A. Hajivassiliou, K.B. Carter, I.G. Finlay, D.G. Young,
Scottish Surgical Pædiatric Society, Stirling, May 1994.

5. Does anorectal angle contribute to fæcal continence?

Association of Coloproctologists of Great Britain and Ireland,
C.A. Hajivassiliou, K.B. Carter, I.G. Finlay,
Royal Society of Medicine, London, June 1994.

6. The development and testing of an artificial anal sphincter.
C.A. Hajivassiliou, K.B. Carter, W. Richardson, I.G. Finlay,
West of Scotland Surgical Association, Glasgow, October 1994.
7. The paediatric surgical applications of an artificial sphincter prosthesis.
C.A. Hajivassiliou, K.B. Carter, I.G. Finlay, D.G. Young,
Royal Hospital for Sick Children Staff Association, Glasgow, December
1994.
8. The Glasgow Neosphincter.
C.A. Hajivassiliou, K.B. Carter, D.G. Young, I.G. Finlay,
Royal Medico-Chirurgical Society, Glasgow, March 1995.
9. A new method of estimating tissue blood flow: a Laser Doppler flow scanner
Prototype.
K. Greer, *C.A. Hajivassiliou*, K.B. Carter, I.G. Finlay, T. Fisher,
Medical Bioengineering Conference, Glasgow March 1995.
10. Towards a prosthetic anal sphincter.
C.A. Hajivassiliou, K.B. Carter, I.G. Finlay,
Scottish Society of Coloproctology, Stirling, March 1995.
11. Non-invasive colonic blood flow measurement.
C.A. Hajivassiliou, K. Greer, A. Fisher, D.G. Young, I.G. Finlay,
Scottish Surgical Paediatric Society / Royal College of Surgeons of Edinburgh
Scientific Meeting, Aberdeen, May 1995.

12. The development and testing of an artificial anal sphincter.

C.A. Hajivassiliou, K.B. Carter, I.G. Finlay,

Association of Surgeons of Great Britain and Ireland Annual Meeting

London, June 1995.

13. Assessment of a prototype Laser Doppler flow scanner.

C.A. Hajivassiliou, K. Greer, A. Fisher, D.G. Young, I.G. Finlay,

Scottish Surgical Pædiatric Society, Glasgow, November 1995.

14. The pædiatric applications of a new Laser Doppler flow scanner.

C.A. Hajivassiliou, K. Greer, A. Fisher, K.B. Carter, I.G. Finlay, D.G. Young,

Royal Hospital for Sick Children Staff Association, Glasgow, December

1995.

15. Non-invasive colonic blood flow measurement in inflammatory bowel
disease *versus* controls.

C.A. Hajivassiliou, K. Greer, A. Fisher, K.B. Carter, I.G. Finlay,

Royal College of Surgeons of Edinburgh Annual Clinical and Scientific

Meeting, Edinburgh, May 1996.

Publications

This Thesis has been composed *de-novo* as opposed to collating and modifying a collection of published papers. The relevant sections of this work were subsequently modified and submitted to the appropriate journals as shown below.

The results of the experiments pertaining to the development of the artificial sphincter could not be disclosed for legal reasons during the period that the International Patent application was being considered. The patent has now been granted in Europe and Australia, and the process for North America is nearing its completion. This has delayed the submission of most of the papers outlined below as they included details of the device to a greater or lesser extent.

The details of the new control pump are still confidential and this work has not yet been disclosed or published.

1. Hajivassiliou C.A., Carter K.B., Finlay I.G.: Anorectal angle contributes to faecal continence.

Accepted as abstract in Int. Journal of Colon and Rectal Disease.

British Journal of Surgery, Vol. 83 (1): Jan. 1995, pp 53-56.

Based on Chapter 1.

2. Hajivassiliou C.A., Carter K.B., Finlay I.G. Assessment of a novel prosthetic Anal Sphincter in an animal model. Submitted to: Diseases of Colon and Rectum.

Based on Chapter 6

3. Hajivassiliou C.A., Carter K.B., Richardson W., Finlay I.G. A novel artificial anal sphincter.

Submitted to: The Journal of Medical Engineering and Technology.

Based on Chapter 3.

4. *Hajivassiliou C.A., Carter K., Finlay I.G.* Measurement of colonic blood flow in the minipig by Laser Doppler.
Submitted to: Journal of Laboratory Animal Science.
Based on Chapter 4.
5. *Hajivassiliou C.A., Grier K., Fisher T., Finlay I.G.* Assessment of colonic blood flow distribution in the human by a new Laser Doppler flow scanner.
Submitted to: The British Journal of Surgery.
Based on Chapter 8.
6. *Hajivassiliou C.A., Grier K., Fisher T., Finlay I.G.* The effects of an artificial anal sphincter on colonic blood flow distribution in the human.
Submitted to: The British Journal of Surgery.
Based on Chapter 8.
7. *Hajivassiliou C.A.* A review of artificial urinary continence devices.
Submitted to The British Journal of Urology.
Based on INTRODUCTION AND HISTORICAL PERSPECTIVE.
8. *Hajivassiliou C.A.* A review of 4000 complications associated with the AMS 800 artificial urinary sphincter.
Submitted to The British Journal of Urology.
Based on INTRODUCTION AND HISTORICAL PERSPECTIVE.
9. *Hajivassiliou C.A., Carter K.B., Finlay I.G.* Assessment of an artificial stool substitute for radiological investigations.
Submitted to: Coloproctology.
Based on Appendix 2.
10. *Hajivassiliou C.A., Young D.G., Hollman A., Finlay I.G.*
Radiological assessment of an artificial anal sphincter in a minipig model.
Submitted to: Radiology.
Based on Chapter 7.

11.*Hajivassiliou C.A.*, Finlay I.G.

A new control pump for the control of artificial sphincter devices.

Patent pending. Submitted to the UK and European Patent Offices.

Based on Appendix 3.

Awards

1. Caledonian Society of Gastroenterology Astra Prize, February 1994.
2. West of Scotland Surgical Association Research Prize, October 1994.
3. Royal Hospital for Sick Children Staff Association Prize, December 1994.
4. Royal Medico-Chirurgical Society of Glasgow Research Prize, March 1995.
5. Department of Trade and Industry, S.M.A.R.T. Award, August 1995.
6. Royal Hospital for Sick Children Staff Association Prize, December 1995.
7. Association of Surgeons of Great Britain and Ireland **Moynihan Prize 1995.**

Outline and organization of this Thesis

The first part of this thesis is a collection of review chapters on the subjects of faecal continence, incontinence and attempts to achieve continence artificially. The complications of a device generally accepted as an option for the treatment of urinary incontinence are reviewed both from the literature, and the reports to the Federal Drug Agency (FDA) in the USA of over 4000 complications.

The first section describes the design of the device and its *in-vitro* evaluation. Some of the engineering parameters assessed both *in-vivo* and *in-vitro* are also presented in this section.

The second section describes the acute and long term animal experiments and results, while in the third section the results of acute experiments on the effects of the device on the blood flow distribution in human colon are presented.

The main thesis concludes with some thoughts on future experiments and technological developments.

A series of six appendixes follows in the last section. These can be read independently and summarize mainly pure and applied mathematical models of fluid flow and rheological evaluation experiments, engineering considerations on the design of this device and reviews of previously patented devices. Most of the experimental data appear in Appendix 4. Appendix 5 presents all the survival clinical and system engineering data for each animal: the clinical data are analyzed in Chapter 6 and the engineering data of the assessment of the device is presented in Chapter 3. In two cases (AMS complication review and sphincter assessment data in Chapter 3) the raw data would occupy several hundred pages. These data are included on 3.5" computer discs appropriately labeled. It should be noted, however, that this cannot protect the files from unauthorized access or tampering and the author has kept appropriately backed up files.

An outline of the contents of the thesis is presented in a short table of contents at the start, whereas a detailed table of contents appears at the end.

INTRODUCTION AND HISTORICAL PERSPECTIVE

***A Review of the Physiological Fæcal Continence
Mechanisms***

***Is conventional surgery satisfactory for the correction of
fæcal incontinence?***

Attempts to achieve continence artificially: A Review

***A successful continence device? Review of 4000
complications associated with the AMS 800 Artificial Urinary
Sphincter***

Γυνή: ὁ δὲ Θεὸς ὑμῖν οὐ προσήειν;

Καρίων: οὐδέπω, μετὰ τοῦτο δ' ἤδη· καὶ γελοῖον δῆτά τι ἐποίησα·
προσιόντος γὰρ αὐτοῦ μέγα πάνυ ἀνέπαρδον· ἡ γαστήρ γὰρ
ἐπεφύσητό μου.

Γυνή: ἦ πού σε διὰ τοῦτ' εὐθὺς ἐβδελύττετο.

Καρίων: οὐκ, ἀλλ' Ἰασὼ μὲν τις ἀκολουθοῦσ' ἅμα ὑπηρυθρίασε
χὴ Πανάκει' ἀπεστράφη τὴν ῥῖν' ἐπιλαβοῦσ'· οὐ λιβανωτὸν γὰρ
βδέω.

Wife: Did not the God approach you?*

Carion: Not till later. And then I did a thing that will make you laugh. For as he
neared me, by some dire mishap my wind exploded like a thunder-clap.

Wife: I guess the God was awfully disgusted.

Carion: No, but Iaso blushed a rosy red and Panacea turned away her head
holding her nose: my wind's not frankincense**.

Aristophanes *Plutus* (lines 696-703).

*: The God was Asclepius.

**:: Iaso, Panacea and Hygieia were daughters of Asclepius.

A Review of the Physiological Fæcal Continence Mechanisms

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Introduction

There is no generally acceptable definition of anal continence that can be applied to all ages and all patients; also, what is considered normal may vary. Absolute control of rectal contents is not present in all normal individuals. The incidence of minor deficits in a control population without anorectal complaints was found to be approximately 10% ¹. The usual clinical definition of continence is based on the absence of faecal soiling, but this may be difficult to establish depending on the degree of cleanliness of the subject being questioned. A score of faecal incontinence was reported by Miller et al², which relates to both the frequency and consistency of the stool (Table 1). Control of flatus in some societies may not be socially necessary. Anal incontinence is not a life threatening disease (in fact it is not a diagnosis, it is a symptom) but it is a socially devastating condition. Many patients do not seek medical advice and thus suffer social alienation and serious psychiatric isolation. As a consequence, reliable epidemiological data on incontinence is unavailable and its incidence is, therefore, underestimated^{1,3,4}.

	Flatus	Fluid	Solid
Incontinence less than once a month	1	4	7
Incontinence between once a month and once a week	2	5	8
Incontinence more than once a week	3	6	9

Table 1: Faecal incontinence score².

Faecal continence in the human depends upon the coordinated action of the anal sphincters which produce circumferential occlusion, and the pelvic floor musculature (especially the puborectalis) which produce angulation between the rectum and anal canal. Other factors which are important in maintaining continence

include: the consistency of the stool⁵⁻⁷, the capacity of the rectum⁸⁻¹¹, normal recto-sigmoid motility^{12,13}, the preservation of a normal sampling reflex¹⁴⁻¹⁶, normal anorectal sensation^{14,17-21}, normal resting anal tone^{13,22,23}, preservation of anorectal angulation (see Chapter 1) and resistance to opening of the anal canal²⁴. The normal anorectal function parameters are summarized in Table 2²⁵ (methodology of measurements summarized by Corman²⁶ and Keighley and Williams²⁵).

	Incontinent	Normal
Maximum resting anal pressure, cmH ₂ O (mmHg)	58 (42.6)	87 (64)
Maximum squeeze anal pressure, cmH ₂ O (mmHg)	120 (82.2)	193 (142)
Rectoanal inhibitory reflex present (%)	31	100
Anocutaneous reflex present (%)	47	100
Threshold rectal sensation (ml)	42	29
Maximum volume retained (ml)	268	>400
Basal sigmoid pressure, cmH ₂ O (mmHg)	44 (32.3)	27 (19.8)
Motility index	680	320
Transit markers passed in 5 days (%)	76	75
Resting anorectal angle (°)	123	88
Pelvic floor descent at rest (cm)	+2.2	-0.4
Pelvic floor descent during straining (cm)	+0.6	-4.3
Anal sensation threshold: midzone (mA)	13.7	5.3
Rectal emptying: % passed in 1 minute	75	75
Saline infusion: volume of first leak (ml)	180	960
Pudendal nerve terminal motor latency (ms)	2.4	2.0
Fiber density in puborectalis	1.7	1.4

Table 2: Changes in anorectal function in idiopathic faecal incontinence²⁵.

Anatomical considerations^{26,27}

Our present knowledge of the pelvic floor is based largely on the meticulous dissections and observations of Thompson (1899)²⁸, Milligan and Morgan (1934)²⁹, Golligher et al (1955)³⁰, Parks (1956)³¹ and Kerremans (1969)³², based on cadaveric dissections and intraoperative observations³¹.

The anorectal region is of dual embryological origin: the visceral inner tube comprises mucosa, submucosa, circular and longitudinal muscle, the latter being thickened caudally to form the internal anal sphincter (Milligan and Morgan 1934²⁹). The outer tube consists of the skeletal muscle comprising the funnel like levator ani muscles and, more caudally, the external anal sphincter (Parks 1975³³).

The anal canal

The anal canal commences at the anorectal angle and ends at the anal verge. It is 3-4 cm long. The lower canal and transition zone are richly innervated with sensory nerve endings²⁷ and surrounded by a complex of sphincters (external and internal). The two concentric cylinders which form the anal canal are shown in Figure 1. The anal canal appears to have a slit-like anteroposterior cross section radiologically³⁴. This may be explained by the anteroposterior attachments of the middle part of the external sphincter (perineal body and coccyx respectively). Kerremans³² and Duthie³⁵ report that the caudal part of the sphincter is attached to the coccyx as well, and Shafik³⁶⁻⁴¹ reports a triple sling arrangement (Figure 2): This involves a three-loop system with two U-shaped loops directed anteriorly and one posteriorly. The top loop arises and inserts on the pubis and is made up of the deep external sphincter and puborectalis. The middle loop attaches to the coccyx (superficial anal sphincter). The lower loop inserts in the anterior perianal skin. His anatomical (gross and microscopic) descriptions are based on post-mortem dissections of a small number of subjects reported in the above series of papers. He subsequently reported that each "loop" can achieve continence independently if intact⁴⁰.

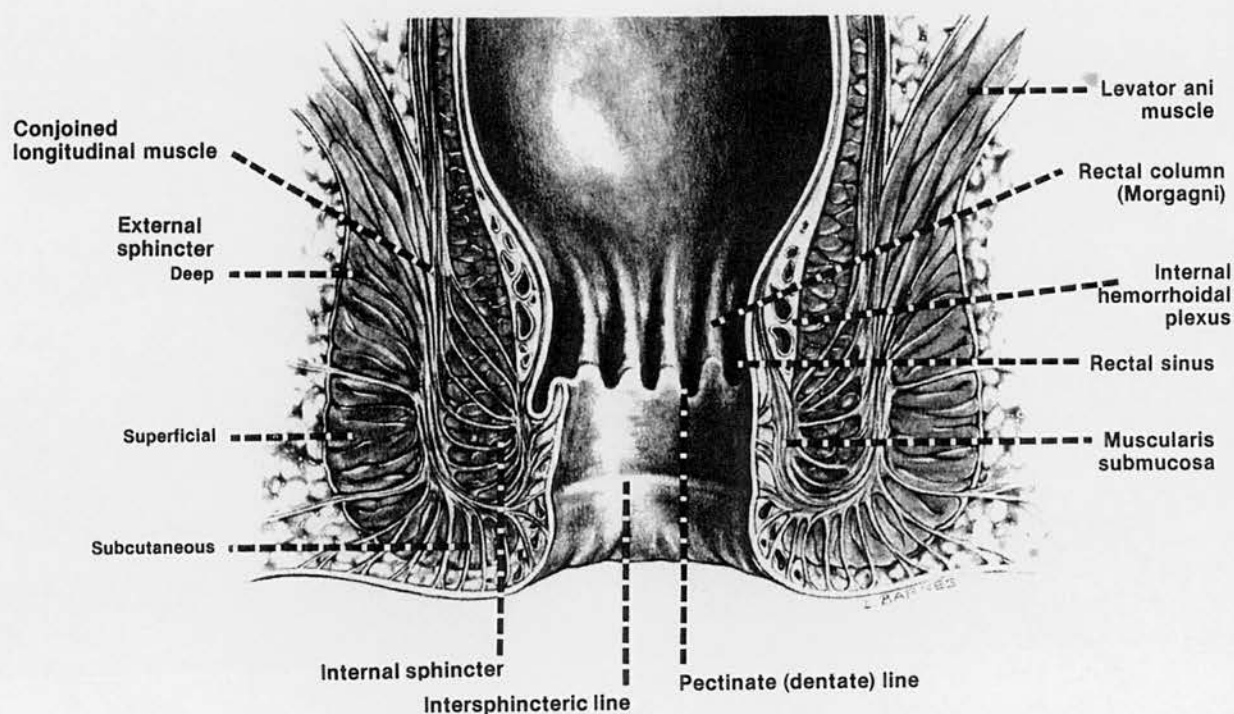


Figure 1: Anatomy of the anal region (reproduced from Corman²⁶).

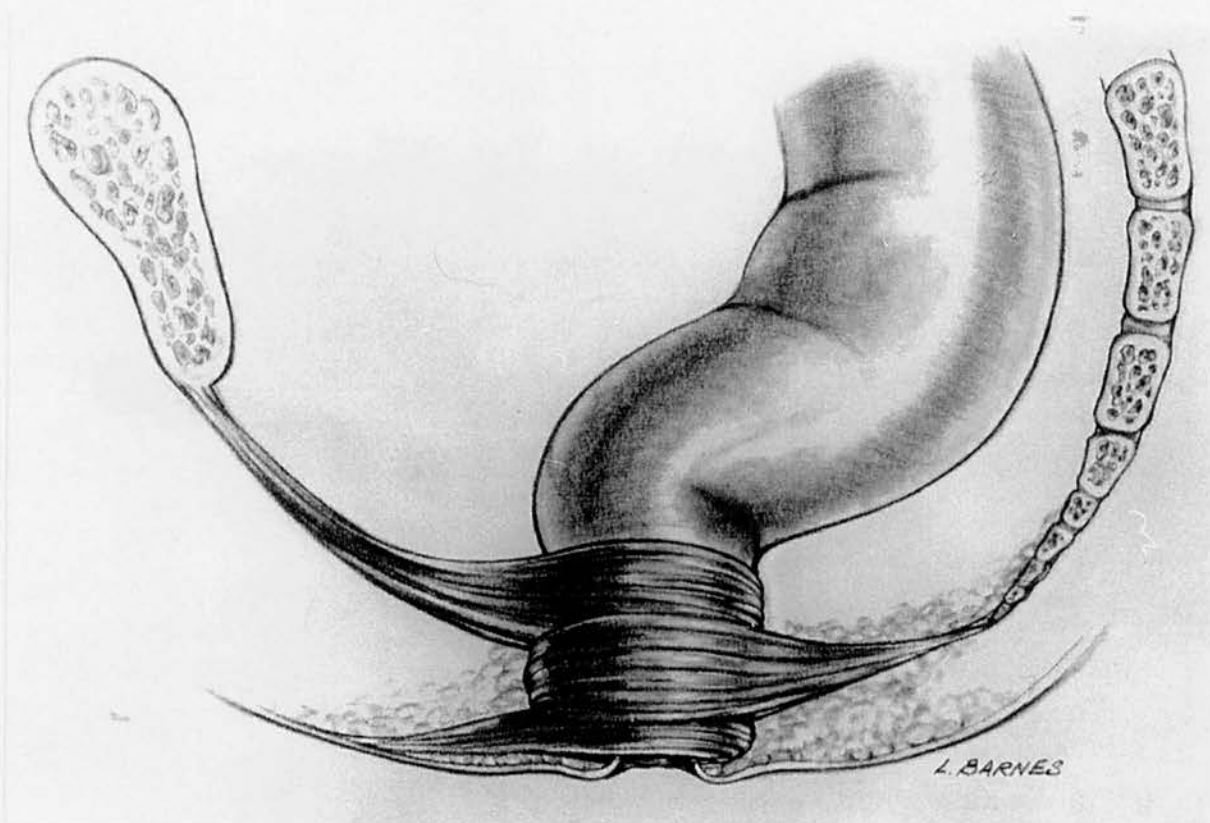


Figure 2: The triple loop system of Shafik³⁶⁻⁴¹. Reproduced from Corman²⁶.

While it is an interesting concept, this theory serves more to obfuscate than to clarify the issues of pelvic floor anatomy and muscle control. In addition, Shafik's findings have not been confirmed by other investigators⁴².

The external anal sphincter

The external sphincter is part of a composite striated muscle encircling the anal canal that enables voluntary control of continence. It is arbitrarily divided into three parts: subcutaneous, superficial and deep (Figure 1). This distinction is of little practical importance as none of these parts is recognizable surgically.

It is recommended that it be

. . . relegated to the junkyard of anatomic trivia where it may languish for the sake of the historical anatomist or the rare individual who spends time carving out the most meticulous dissections. (Dalley, from Corman 1993²⁶).

Kerremans³² suggested that the different interpretations of the anatomy of this muscle may be due to the variability of the fibrous sheaths which appear to subdivide it. Posteriorly, the upper fibers of the external sphincter merge with the inner fibers of the puborectalis.

The internal anal sphincter

The internal sphincter is the continuation of the distal portion of the circular muscle of the rectum which is thickened to ≈ 2 mm at that level^{27,35}. It is 2 to 4 cm long³⁵. In the descriptions of Milligan and Morgan²⁹ the internal anal sphincter does not reach the anal canal. This has been disputed by Eisenhammer⁴³ and this later confirmed by other workers^{30,44}.

The levator ani

This muscle was first described by Vesalius⁴⁵, as “Duo musculi intestinum post egestionem sursum trahentes” (Figure 3). It arises from the bony pelvis and the obturator fascia and spreads out in a funnel like manner to form a thin muscular pelvic floor (Figure 4). For practical purposes, each levator ani may be regarded as consisting of two main parts: the pubococcygeus with its specialized portion the puborectalis and the iliococcygeus (Figure 4, A and B). The pubococcygeus and puborectalis arise from the posterior aspect of the pubis and from the white line as far back as the obturator canal. The pubococcygeus fuses with its fellow posteriorly to form part of the anococcygeal raphe. Its inner portion is thickened and forms the puborectalis which arises from the symphysis pubis. These fibers surround the prostate (or vagina) and the anorectum, meeting fibers from the opposite side in a loop or U-shaped girdle (Figure 4). Apart from the external sphincter, the puborectalis blends with the longitudinal muscle and the adjacent part of the internal

sphincter (Figure 1). The iliococcygeus is a thin muscle which supports the pelvic outlet.

Contraction of the levator ani and the puborectalis sling pulls the anorectal junction upward and forwards, elongating the anal canal and increasing angulation between the anal canal and the rectum¹³. This, along with contraction of the external and/or internal anal sphincters results in effective closure of the anal canal.

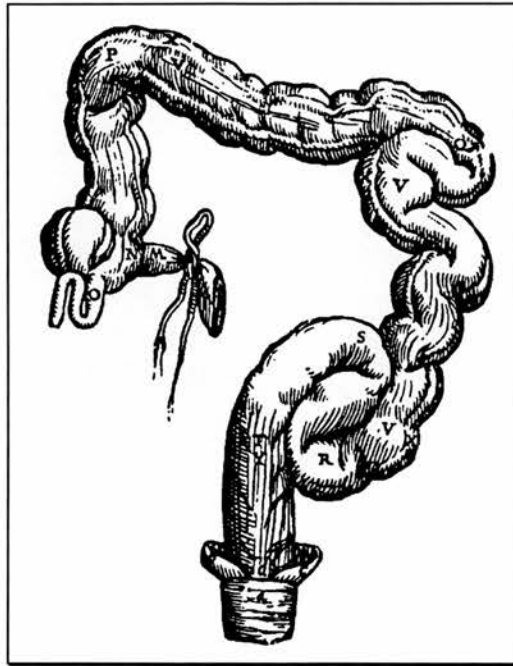
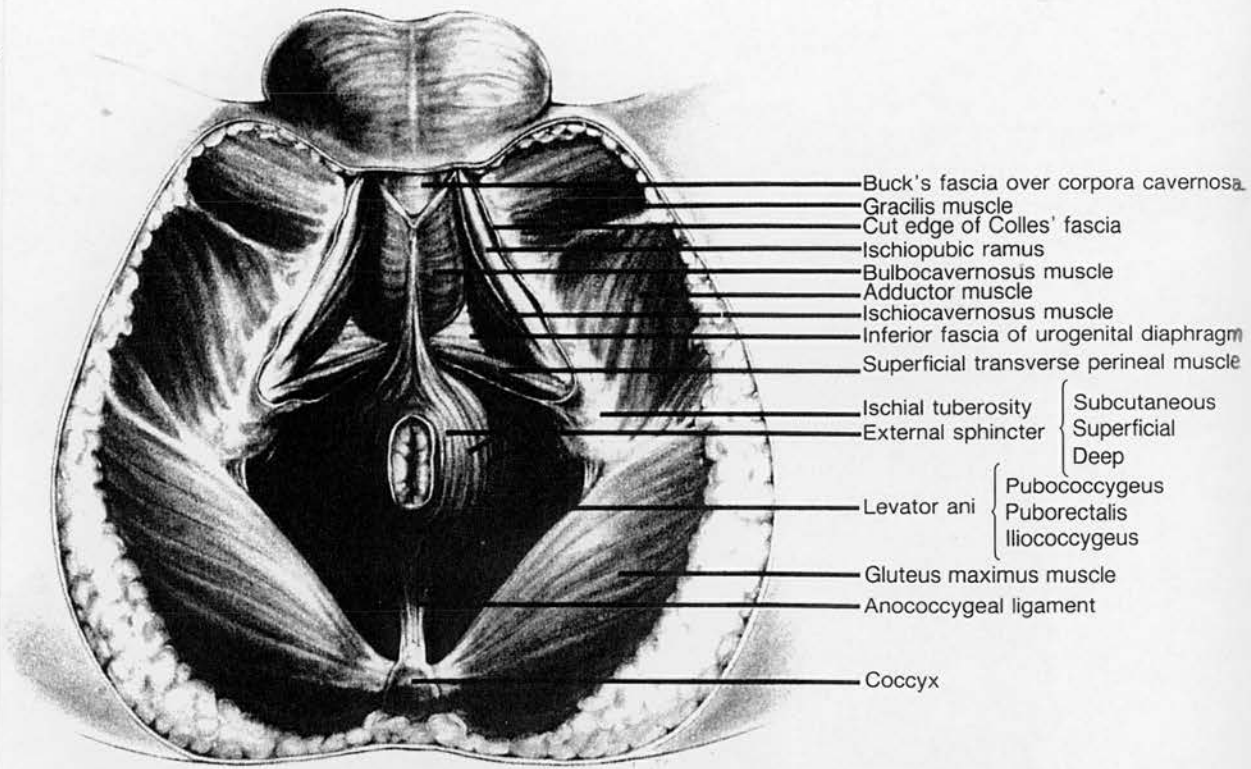


Figure 3: The Anal Sphincters (Special Muscles of the Rectum), reproduced from: The Illustrations from the Works of Andreas Vesalius⁴⁶, plate 55:4.

A.



B.

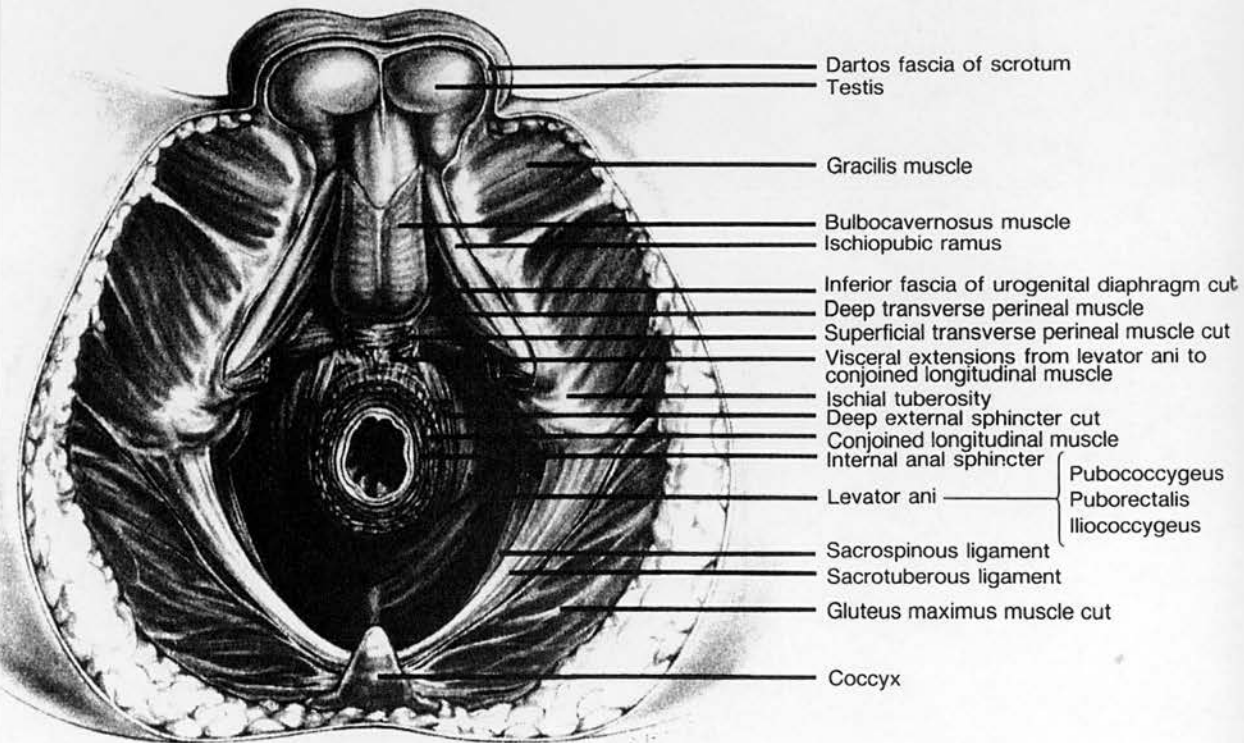


Figure 4: Anatomy of the male perineal musculature:
A. Inferior view with the skin and subcutaneous tissues removed.
B. Exposure at the level of the midanal canal (from Corman 1993).

Somatic and visceral innervation of the pelvic floor:

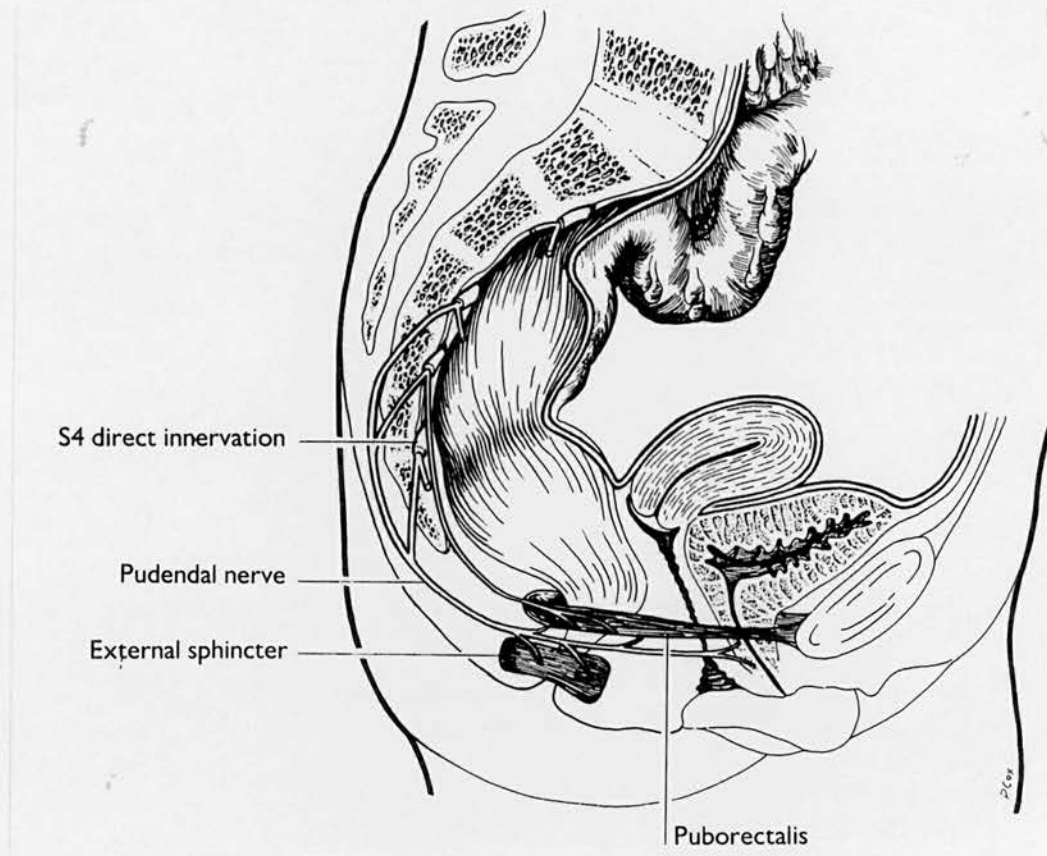


Figure 5: Sagittal section of the female pelvis to show the innervation of the anal sphincters and puborectalis (reproduced from Keighley and Williams 1993⁴²)

Somatic innervation

The striated muscles of the pelvic floor are innervated by the S2, S3, S4 motor nerve roots²⁷. The external anal sphincter, as well as the peripheral part of the levator ani, is supplied by the pudendal nerve (Figure 5). It also carries afferent nerves from the anal canal and perianal skin. The puborectalis is supplied by the perineal branch of S4, which also carries afferent fibers from the anal canal and perianal skin. The levator ani, therefore, has dual nerve supply: it is supplied by the pudendal nerve (peripheral part) and perineal branches of S3 and S4 (the branch of S4 supplies the puborectalis).

Percy et al (1981)⁴⁷, demonstrated the functional innervation *in-vivo* in 20 patients. In their experiments, the direct branch of the sacral nerves S3 and S4 was identified on the visceral surface of the levator ani and puborectalis during the operation of postanal perineorrhaphy. These branches were electrically stimulated and the evoked responses recorded using a concentric needle electromyography (EMG) electrode placed in each component of the pelvic floor musculature (pubococcygeus, puborectalis, and the upper and lower parts of the external anal sphincter). Stimulation evoked action potentials from the pubococcygeus in all 20 cases and the puborectalis in 19. No evoked EMG activity was detected from the external sphincter muscle on either side.

The response to stimulation of the pudendal nerves was studied in addition in three patients. Evoked activity was recorded in the ipsilateral external sphincter but not in the components of the levator ani. Moreover in these three patients there was no overlap in the parts of the pelvic floor supplied by the pudendal nerve and the direct branches of S3 and S4. Their results suggest that the pudendal nerve does not normally innervate puborectalis and document that this muscle is predominantly innervated by the direct branches of S3 and S4.

Afferent somatic innervation is abundant and varied from about 10-15 mm above the anal valves, down to the boundary with hairy skin. Somatic sensation (touch, pin-prick, heat and cold) was demonstrated to be perceived in the anal canal to a level 2.5-15 mm above the anal valves⁴⁸. This was suggested to be important in the discrimination between solid, liquid and gaseous contents¹⁴.

Visceral innervation

Parasympathetic innervation to the rectum/internal sphincter (visceral inner tube) is supplied by the nervi erigentes (S2-4) via the presacral nerves, and sympathetic from the hypogastric plexus along the inferior rectal artery^{27,42}. Nociceptive pathways travel in both parasympathetic and sympathetic systems via the inferior and superior hypogastric plexus to the ganglions at L1 and L2. The

sensation of rectal distention travels with the pelvic splanchnic nerves to S2 and S3. It appears that this may be mediated by receptors found both in the rectal wall and pelvic floor fascia / musculature, as this sensation is not completely abolished by rectal resection and coloanal anastomosis⁴⁹.

Physiological considerations

In this section, the function of the anal canal, the sphincter mechanisms and the pelvic floor muscles will be described.

The physiological mechanism of the pelvic floor is designed to accomplish the following two tasks:

- To convert a potential perineal colostomy into an automatically functioning sphincter controlled anus.
- To resist intra-abdominal pressure forces which, if unopposed would tend to produce herniation of the perineum³³.

The anal canal is anatomically 3-4 cm in length and is normally closed at rest and during sleep⁵⁰. A high pressure zone is present in the anal canal (Table 2), and this is maximal at about 2 cm from the anal verge³⁵. This high pressure zone is present in both term and pre-term infants and its length is 14.7 ± 2.9 mm and 10.3 ± 2 mm respectively⁵¹. There have been recent reports of attempts to plot the spatial distribution of the pressures inside the anal canal by using a multi-channel water perfused pressure measuring station pullthrough setup and presenting the results as a vector diagram⁵² (Figure 6). The area of the polygon is a reflection of the net

pressure at a specific level in the anal canal. The pressure vector volume at a specific level is the area multiplied by the distance between stations.

The results shown in Figure 6 do not represent true pressure distributions in the authors' opinion for the following reasons:

- It is impossible according to engineering laws for a system in equilibrium to have a heterogeneous pressure distribution along any axis. If the pressure was indeed greater posteriorly than anteriorly, the posterior rectal wall would move towards the area of lower pressure until the pressures equalize and at this point the movement would cease.
- The presence of the thick perfused catheter upsets the basal pressure characteristics of the anal canal⁵² and, due to the tube's low compliance and lack of compressibility, does not allow effective pressure transmission to the anterior rectal wall.
- The path of the pulled-through catheter is not straight but follows the curve of the anorectal junction. It is well known that pressure measuring catheters are unreliable in directional measurements under these circumstances as the application and relative sealing of the pressure measuring area of the catheter against the mucosa would lead to an artificially high reading.

What this method probably demonstrates is the direction from which active pressure is being applied (e.g. posteriorly by the puborectalis or caudally and anteriorly when the anterior part of the catheter abuts on the area of the pubis) and also the fact that

part of this exerted pressure is being dissipated by the catheter so that only a fraction is transmitted to and measured at the other side.

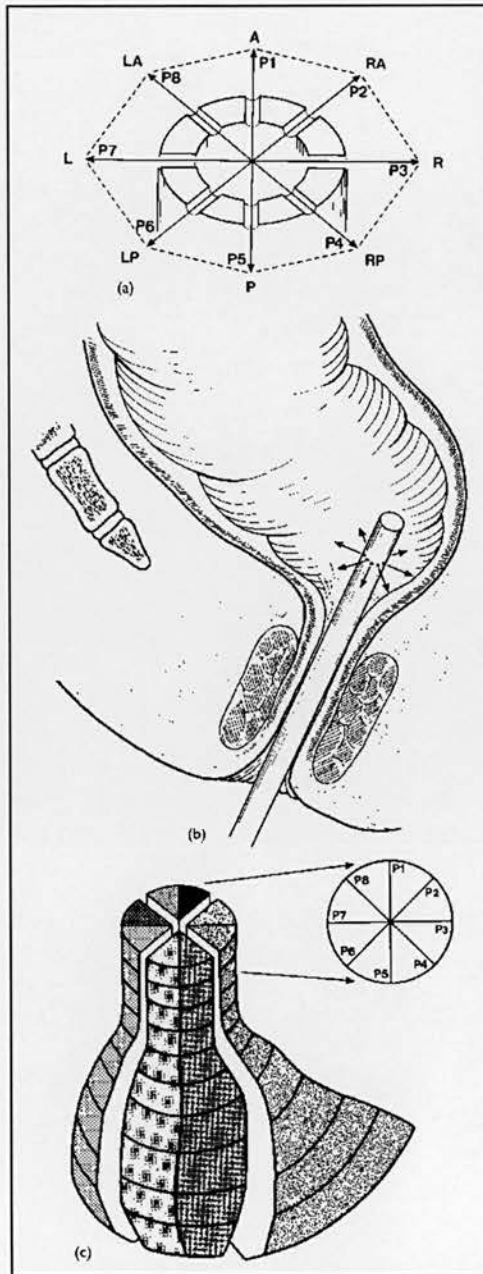


Figure 6: Vector diagram of anal pressures⁵². Reproduced from Keighley and Williams²⁵.

- (a) The eight port perfused catheter. A, anterior; P, posterior; L, left; R, right.
- (b) The station pullthrough anal manometry probe placed in the rectum.
- (c) An eight quadratic wedge of the pressure vectogram.

Mechanical properties of the anal canal

In a theoretical evaluation to describe the mechanical properties of the anal canal region, Gibbons et al⁵³ modeled the anal sphincter complex by a two tube model, with a luminal diameter = d . The outside cylinder represents the external anal sphincter and the inside the internal sphincter and mucosa. The basic assumptions made are that when the “anal cylinder” layer is lax, tension is zero and that sphincter pressure solely depends on the outside layer. Tension *versus* diameter were predicted to vary linearly and this was confirmed experimentally^{52,53}. The situation at the limits (i.e. $d=0$) may not be completely accounted for by the initial assumptions made by the model: The anal canal pressure was measured with probes of different diameters and the anal sphincter tension estimated⁵². The measurements were performed at rest, maximal pelvic floor contraction and rectal distention. Estimated tension was plotted and found to increase linearly with probe diameter (i.e. anal distention). When all three lines were extrapolated to the origin, zero tension was predicted at approximately 1.5 mm of internal anal diameter for all three (rest, maximal pelvic floor contraction and rectal distention).

In the above theoretical model⁵³, the luminal pressure is predicted to fall to zero before the diameter is zero. The “autoregulatory thickness adjustment” was thus proposed, which allows for the diameter to fall to zero passively. It was, therefore, proposed that this function of passively occluding the diameter of the anal canal at rest is achieved by the passive engorgement of the anal canal cushions^{52,53}. The anal canal would subsequently resist passive opening^{24,53}.

The muscles of the anal canal:

Internal anal sphincter

The internal sphincter (IAS) is in a continuously tonic state^{13,32}, and provides the most important component of resting anal pressure when the anal canal is closed^{22,23}. This contribution is reported to be between 50%²² and 85%²³ at rest. Shafik⁵⁴ suggests that the IAS is not at maximal contractility at rest, especially since its contractility is reportedly improved by biofeedback⁵⁵⁻⁵⁷; this is probably true but cannot be surmised from the method of stimulation he described⁵⁴, as the EAS may also have been stimulated at the same time.

The IAS muscle exhibits continuous activity which is both under autonomic control and locally mediated by an intermyenteric plexus (since circular rectal myotomy abolishes activity²⁵). Myogenic activity has also been reported *in-vitro*^{58,59} and was indistinguishable from that of more proximal rectal muscle⁵⁸. Electrical activity consists of slow (16 per minute) and ultra slow waves (1.6 per minute), but this does not correlate directly with pressure activity³². The activity of the smooth muscle component is completely inhibited by rectal distention: the rectoanal inhibitory reflex^{12,13}. This reflex is present in both term and pre-term infants⁵¹. Resting anal pressure is decreased when 0.2% solution of glyceryl trinitrate was applied locally⁶⁰. This supports the hypothesis that nitric oxide is the final mediator in IAS relaxation suggested by animal *in-vitro* experiments⁶¹, animal *in-vivo*⁶² and human studies⁶³. Direct demonstration of a descending nitrergic rectoanal pathway was described recently⁶⁴. The *in-vitro* responses of the smooth muscle components of the anorectal region are summarized in Table 3⁵⁹ confirming sphincter subspecialisation.

	Myogenic Tension	Muscarinic response (Carbachol)	α-adrenergic response (Phenylephrine)	β-adrenergic response (Isoprenaline)
Rectal smooth muscle	Absent	Stimulation	Relaxation	Relaxation
Conjoint longitudinal muscle	Present	Stimulation	Stimulation	Relaxation
Internal anal sphincter	Present	Relaxation	Stimulation	Relaxation

Table 3: *In-vitro* response of human rectal and anal muscle to cholinergic and adrenergic neurotransmitters (summarised from O’Kelly et al⁵⁹).

The internal anal sphincter is also important as a means for allowing rectal contents to come into contact with the sensitive anal mucosa during the sampling reflex¹⁴⁻¹⁶. This reflex is deficient in faecal incontinence¹⁵. The function of the internal anal sphincter deteriorates with advancing age^{8,65,66}.

External anal sphincter

Voluntary control of continence is provided by the external anal sphincter and the puborectalis sling. Voluntary contraction is accompanied by rapid recruitment and high pressures are achieved in normal subjects (see Table 2). External sphincter function cannot be sustained and there is rapid fatigue, hence it usually merely provides a final control mechanism if faecal material enters the upper anal canal. Age causes increased fiber density in the EAS⁶⁷, probably as a result of denervation, with a concomitant decrease in its ability to generate occlusive pressure. The external anal sphincter was originally thought to be quiescent at rest and activated only by reflex

mechanisms¹². This hypothesis was subsequently disproved and it is now known that this muscle (and the other striated muscles of the pelvic floor) are electrically continually active even at rest^{13,32}. Their electrical activity varies with the posture and activity of the subject¹³. The resting EMG activity of the external anal sphincter is normal after transection of the spinal cord above the third lumbar segment¹³. During coughing, there was greatly increased EMG activity in the external sphincter which coincided with the rise in intra-abdominal pressure. This suggests that the cough response is part of a reflex mechanism. Cutaneous perianal stimulation excites a reflex response from the external anal sphincter⁶⁸. This response can be elicited in paraplegic patients indicating that cortical control is not involved and that it is a spinal reflex.

A burst of EMG activity preceding the inhibition of the internal anal sphincter is recorded in the external anal sphincter after rectal distention¹⁷. This activity persists throughout the duration of rectal distention in normal subjects but not in patients who suffered cord transection above the lumbar segments²³. This phenomenon has been termed constant relaxation³².

Upon straining, different EMG responses of the EAS are observed³² in different subjects:

1. Sudden abolition of all electrical activity (also reported by Parks¹³)
2. Initial burst of EMG activity, followed by inhibition throughout the period of straining
3. Persistent increased EMG activity
4. Bursts of polyphasic potentials.

Distention of the anal canal (both digitally and by a balloon) was reported to elicit a burst of EMG activity in the EAS followed by some decrease and finally a sharp increase when the distention ceased⁶⁹. The latter response was called the closing reflex⁶⁹. In paraplegic subjects, after the brisk increase in muscular activity, complete inhibition ensued for the duration of anal distention⁶⁹. This suggests that,

in normal subjects the inhibitory reflex is overshadowed by cortical excitatory EAS activity.

The above descriptions were sequentially presented to follow the temporal pattern of defaecation (rectal distention, straining, distention of the anal canal). It is now clear that the normal defaecatory response involves inhibition of the pelvic floor musculature in most instances⁷⁰, so it is unlikely that the excitatory activity seen during anal distention is part of normal rectal evacuation. How closely the pattern of muscle activity seen during straining and anal distention resembles the situation during actual defaecation is difficult to determine. The presence of an observer peering at the perineum together with an EMG needle electrode can hardly be construed as mimicking the events of normal defaecation.

Levator ani (Puborectalis)

The levator ani form a cradle for the rectal ampulla. Like the external anal sphincter they are tonically active at rest^{32,69,70}. The puborectalis is almost a sphincter anatomically, apart from the anterior 3 cm of its circumference which is made up by the pubic arch (Figure 4). The puborectalis in fact acts as a powerful sphincter of the upper part of the anal canal³³ its forward pull creating the anorectal angle. The puborectalis has an important sensory function in that stretching of its fibers leads to the urge to defaecate³³.

Anorectal angulation is only present in adults and orthognate apes. It is absent in the newborn and quadruped animals³². The forward pull of the puborectalis is responsible for the anorectal ring palpable on rectal examination at the upper anal canal. Contraction of the puborectalis sling decreases the anorectal angle and pulls the anorectal junction towards the pubis. This action effectively closes the upper anal canal^{32,33,71}.

Kerremans³² and Ihre⁷⁰ showed that during voluntary contraction of the pelvic floor musculature, coughing or straining, the external anal sphincter and puborectalis

showed almost identical electrophysiological characteristics suggesting that the two muscles function as a single unit.

Conclusions

Muscles which are activated only voluntarily would be useless for the task of maintaining continence as a person's attention would constantly have to be directed to them. The automatic mechanism as indicated above is due to reflex activity. The pelvic floor muscles are truly postural in that they are continuously active at rest (the anal sphincter of quadruped animals is a fast twitch muscle⁷² as opposed to its counterpart in the human). The reflex arc is made up of stretch receptors in the pelvic floor muscles, an afferent neuron passes to the spinal cord, and an efferent motor neuron in turn activates the muscle³³.

This reflex mechanism ensures not only that the muscles are constantly in action, but also that their activity alters when a person walks, coughs or laughs. A highly complex interaction between the reflex mechanisms exists to subserve normal continence.

Anorectal Angle and the "Valve" Theories

Anorectal angle

There is a lack of uniformity in defining the anorectal angle (Figure 7) and this, along with the measurement of other anorectal parameters has been standardized by a working party⁷³. Cine-defaecography^{74,75} or video-proctography⁷⁶ appear to give the most reliable estimations of anorectal angle and are superior to balloon defaecography⁷⁷. Some authors have used the angle at the posterior rectal border, while others measure the anorectal angle between the axis of the anal canal and the central axis of the rectum; there is considerable interobserver variation when the first method is used^{78,79} and the latter is reported to be a more reliable technique^{80,81}. Using the central anorectal angle⁷³, the average angle at rest is approximately 80°

(120° in children⁸²). Hip flexion increases this to around 90° . During defæcation this angle opens to about 115° , while squeezing the anus and the Valsalva manoeuvre decrease the anorectal angle to $85\text{-}100^\circ$ (with the angle being more acute during the former action). Changing position from lateral decubitus to sitting straightens the resting angle, with no change from sitting to standing.

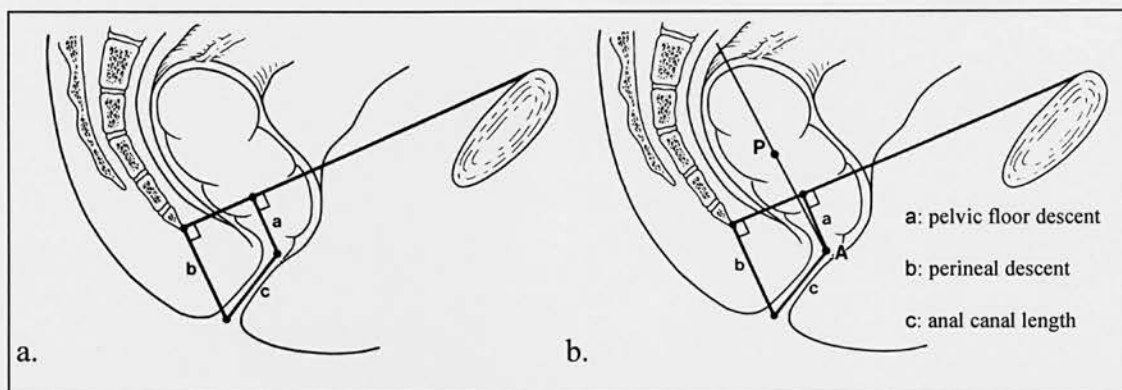


Figure 7: The Anorectal Angle as it appears radiologically^{42,73} during videoproctography. The pubococcygeal line is drawn in both figures. The anorectal angle can be estimated using the long axis of the rectum: angle between lines “a” and “c” in (a.), or the long axis of the rectal centroid: angle between line “PA” and “c” in (b.). The centroid is the centerpoint (P) of the rectal image, such that a line between it and the apex of the anorectal angle bisects the rectal image into two equal areas.

It is generally agreed that the most important element in the system comprising the internal and external sphincters and the levator ani complex is the puborectalis sling^{32,35,71}. Any damage to this muscle results in major defects of continence. This muscle acts as a powerful sphincter on the upper anal canal and also creates the anorectal angle. Kerremans³² observed that the more acute the anorectal angle, the lower the squeeze force required to retain a faecal bolus in the rectum. The role of this angulation in the maintenance of continence was investigated experimentally in our laboratory and is discussed in Chapter 1.

Flap valve

One of the major anatomical functions of the anorectal angle was considered to be the creation of the flap valve mechanism at the anorectal junction^{13,33,71}. The mucosa of the lowest part of the anterior rectal wall is forced into the upper anal canal closing it off (Figure 8). This theory has been largely discounted in normal subjects without obstructed defaecation or prolapsing rectum, as radiological observations during the Valsalva manoeuvre showed that the anterior and posterior rectal walls did not appose one another⁸³. In addition, rectal pressures were found to be consistently lower than those generated by the anal canal⁸³ strengthening the conclusion that continence did not depend on 'valvular' mechanisms.

Flutter valve

This theory was proposed by Edwards and Phillips³⁴. They suggested that normal continence was due partly to intra-abdominal pressure being transmitted at the level of the levator ani, laterally to the side of the anal canal in the region of the anorectal junction (Figure 9). The anal canal appears to be an anteroposterior slit³⁴ radiologically and this pressure could compress it in a way similar to a simple flutter valve (Figure 10). This theory was considered unlikely by Duthie³⁵ since although an occlusion was seen radiologically in the anorectal region when the rectum was outlined by barium contrast, puborectalis activity could not be excluded.

Kerremans³² also pointed out that the segment described as acting as a flutter valve lies below the levator ani cradle at the level of the puborectalis sling. The flutter valve mechanism, therefore, could not act by increases in intra-abdominal pressure. In addition the flutter valve could not afford protection when the intrarectal pressure rises. Another weakness of this theory is the fact that, in engineering terms, a flap valve can only function if the conduit it would seal is not continuous (Figure 10).

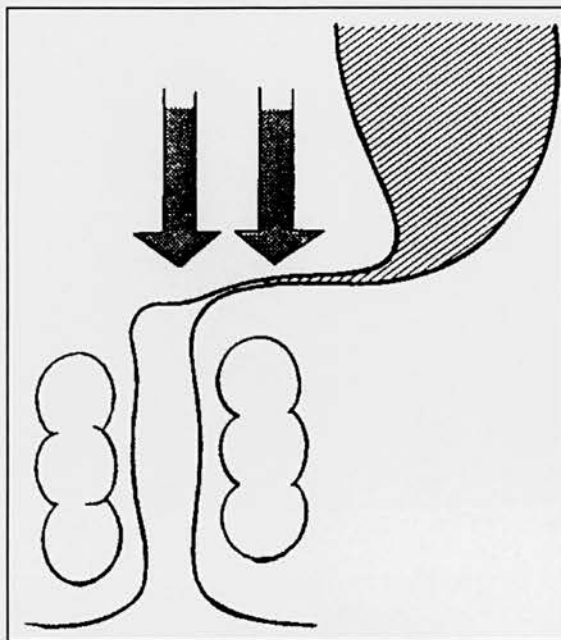


Figure 8: The Flap Valve Theory. Diagram to illustrate how an increase in intra-abdominal pressure was thought to close the anal canal as suggested by Parks³³.

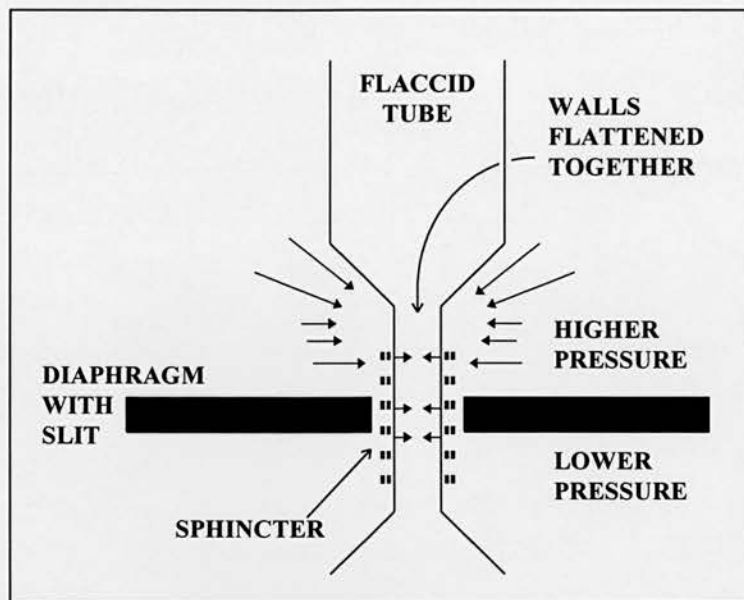


Figure 9: The anorectal flutter valve theory³⁴.

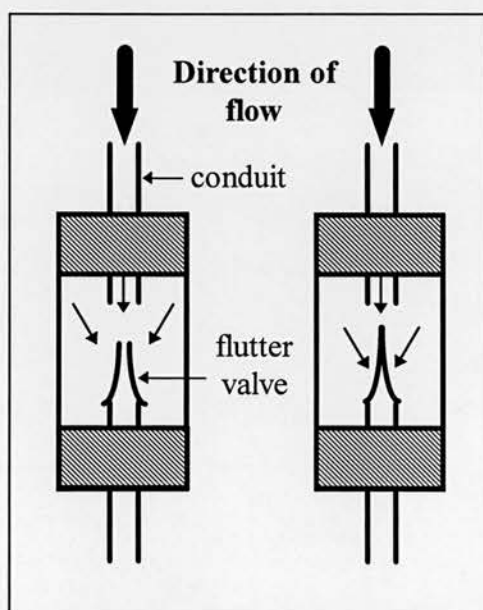


Figure 10: Diagram of a simple flutter valve. In order for the flutter mechanism to be effective, the conduit should be discontinuous at the point of the valve.

A series of simple experiments were conducted *in-vitro* to check the validity of the flutter valve theory (Chapter 2). The results of this study further weaken the flutter valve theory.

A Summary of the Physiology of Defaecation

The mechanism of defaecation is still incompletely understood, despite intensive investigation by several groups of workers. Based on the above descriptions, the act of defaecation would seem to progress as follows: Rectal filling stimulates receptors in the rectal wall, mesentery and pelvic floor musculature, and sampling reflexes allow controlled contact with the upper anal canal. Once a person is aware of the presence of material in the rectum, they need to determine whether defaecation is convenient. If it is not, the lower rectal contents are returned proximally by a strong contraction of the levator ani and the EAS. This allows recovery of the rectoanal inhibition initiated by distal rectal filling and allows the return of IAS tone. If defaecation is desirable, the anal canal opens and pelvic musculature inhibition ensues (rectoanal inhibitory reflex) allowing some degree of pelvic floor descent. This, combined with the squatting position straightens out the axes of the anal canal and rectum, geometrically facilitating rectal evacuation. Intrarectal pressure exceeds anal canal pressure by a combination of rectal contractions and increase in intraabdominal pressure and this results in expulsion of the rectal bolus. Basal sphincter and levator tone returns upon the relief of rectal distention. Release of gas in the presence of other rectal contents can still take place against a partially closed sphincter and an unrelaxed anorectal angle (this would explain the associated characteristic sound). Faecal retention while passing flatus may not be effective if the rectal contents are liquid, because anorectal angle does not enhance continence to liquids (see Chapter 1).

They say Man has succeeded where the animals fail because of the clever use of his hands; yet when compared to the hands, the Sphincter Ani is far superior: If you place into your cupped hands a mixture of fluid, solid and gas and then through an opening at the bottom try to let only the gas escape, you will fail. Yet the Sphincter Ani can do it. It apparently can tell whether its owner is alone or with someone, whether standing up or sitting down; whether its owner has his pants on or off. No other muscle in the body is such a protector of the dignity of man, yet so ready to come to his relief.

Bornemeier

(Quoted in Annals of Surgery
1982, Vol. 195(4):453)

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***Is conventional surgery satisfactory for the correction of
fæcal incontinence?***

“The plight of a patient with frank fæcal incontinence is a very unhappy one indeed. There is the obvious association with uncleanliness and the feeling of being a social outcast. Such a person will not meet people, will not leave the house, or be able to do the shopping. If the situation is known to the family the patient may well be rejected as a result, especially in old age. It is indeed a very grave social problem, particularly with the elderly, and anything that will improve it is highly desirable. The frequency of the problem is greater than is generally realised, because patients will not discuss it and will not even tell their nearest relatives or medical advisors. They manage to cope for some years by wearing a great deal of padding, but finally even this is of no avail.”

The late Sir Alan G. Parks
(President's Address to the Royal Society of Medicine 1975)

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Fæcal incontinence is a common, socially devastating condition which affects all ages and remains a major unresolved clinical problem^{1,2}. The incidence and prevalence are underestimated³, especially in middle aged women in whom child birth injury is the main cause³. The results of conventional surgical correction for fæcal incontinence are disappointing^{1,2}, except in cases of direct trauma to the sphincter⁴. Although postanal repair and primary sphincter overlap repair benefit some patients^{1,2,4}, a proportion subsequently resort to colostomy. Further, patients with severe congenital malformations and anorectal excision surgery have no realistic alternative to stoma diversion⁵.

Aetiology of Fæcal Incontinence

The causes of fæcal incontinence can be either congenital or acquired, the latter being by far the commonest. They can be summarized as follows:

CONGENITAL ANOMALIES

Spinal Dysraphism, Imperforate anus, Hirschprung's Disease, Sacral Agenesis

TRAUMA

Surgical: fistula surgery^{6,7}, hæmorrhoidectomy⁸,
sphincterotomy^{6,9},
sphincter stretch¹⁰, pullthrough operations, low
anastomoses¹¹

Obstetric: perineal tears¹²⁻¹⁴, pressure denervation or damage to
sphincters^{3,15-17}

Accidental: war injury⁴, social injury¹⁸

COLORECTAL DISEASE

*Haemorrhoids*⁸, *Rectal prolapse*¹⁹, *Intussusception of the rectum*²⁰,
Inflammatory bowel disease, tumours

NEUROLOGIC DISEASE

Cerebral: tumour, vascular accident, dementia, trauma

Spinal: tumour, vascular accident, trauma

Peripheral: diabetes mellitus, multiple sclerosis, pudendal nerve injury

Idiopathic ("Neurogenic"): Pelvic floor denervation^{15,16,21,22}

MISCELLANEOUS

Laxative abuse, Diarrhoeal conditions, Fæcal impaction, Encopresis.

Treatment of Fæcal Incontinence

Fæcal incontinence is no exception in that treatment should be directed to its cause. Incontinence attributable to trauma, is most likely to be treated successfully²³. Despite the potential appeal of surgical intervention, however, many individuals can be adequately managed by non-invasive means. Medical treatment should be offered to those who have no antecedent history of trauma, those for whom the potential benefits are problematic, those who are felt to be of high surgical risk and obviously those who decline an operation.

Non-Surgical Treatment of Fæcal Incontinence

The following options are available:

Bowel management program

Perineal exercises

Biofeedback

Electrical stimulation

Anal Plug

Bowel management program

The aim of a bowel management program is to reeducate the bowel to empty regularly and at a predictable time, thus establishing a routine for defæcation that is safe, convenient and dependable. If this is successful, patients with virtually no sphincter control (e.g. with severe congenital abnormalities, spina bifida or trauma) may be spared from the necessity for a diversion procedure. The bowel is kept in a state of controlled constipation and stimulated to empty by the use of laxatives and/or enemas given at regular fixed intervals. Reflex evacuation can be achieved by massaging the abdomen to stimulate peristalsis and also utilizing the gastrocolic reflex. This combination of optimizing fæcal consistency, controlling the time of defæcation and stimulating peristalsis may result in socially acceptable continence in a significant proportion of these patients, in whom a bowel action two to three times a week may be adequate and, in fact, advantageous.

Perineal exercises

Elaborate regimes of perineal muscle exercises have been devised with doubtful results. Exercise can increase the bulk of striated muscle and hence, theoretically, the effectiveness of the external (but not the internal) anal sphincter and puborectalis. It is, however, quite difficult to communicate the instructions of which muscle to contract to the patients and this method has not gained widespread

acceptance on its own. A more effective approach is to combine the exercise program with biofeedback²⁴.

Biofeedback

Operant conditioning or biofeedback involves the measurement of a parameter pertaining to anal sphincter contraction (e.g. pressure²⁵ or EMG²⁶) and allowing the patient a verbal or visual cue as to its effects. There have been numerous publications that attest to the success of biofeedback training for improving continence in idiopathic faecal incontinence²⁵⁻²⁸, in children with spina bifida²⁴ and in conjunction with transcutaneous nerve stimulation in a patient with imperforate anus²⁹. Reports of success in other defaecation disorders include severe constipation in children^{30,31} and adults³² and obstructed defaecation (anismus)³³⁻³⁵. A number of portable biofeedback devices are available commercially. Such a device has been designed by the author as a cheap alternative to the above and is being assessed at the Royal Hospital for Sick Children (Figure 1).

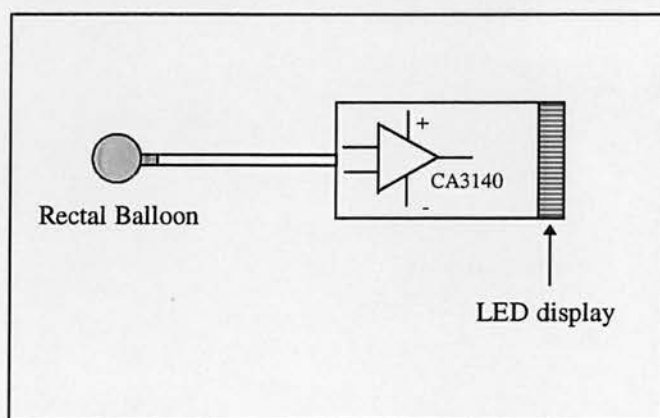


Figure 1: Simple biofeedback unit designed by author. The circuitry involves a standard Baxter pressure transducer and a CA3140 differential amplifier chip. The response is graded on the LED display. The sensitivity of the device is variable (its control is inaccessible to the patient).

Electrical stimulation

Caldwell seems to have been the first to report electrical stimulation of the anal sphincter³⁶. He applied a stimulation current via secondary induction by two electrodes connected to a coil in an attempt to control rectal prolapse. Hopkinson and Lightwood reported their preliminary results on one patient with faecal incontinence using an anal plug electrode for sphincter stimulation³⁷. The device applied a tetanizing stimulation to the anal sphincter and pelvic floor through a plug shaped electrode. They subsequently reported "good" results in nine patients treated with this method³⁸ and similar short term results were reported by other workers³⁹. Although perineal strengthening exercises might accomplish the same goal, the use of electrical stimulation as well^{24,29}, particularly in patients who are unable to understand or perform such exercises, may offer some improvement. Glen⁴⁰ reported "good" results in a series of thirty patients with faecal and urinary incontinence. The paucity of similar reports over the last fifteen years may imply failure or non-acceptance of this method. Brindley⁴¹ first reported an implantable anterior sacral root stimulator to control urinary incontinence and subsequently a pudendal nerve stimulator to control faecal incontinence⁴². The approach of Williams and co-workers whereby, by chronic low frequency stimulation, normal type II fatigueable muscle fibers are transformed to type I fatigue resistant fibers^{43,44} appears to be the most promising. The latter method will be discussed further in the following part of this chapter (Gracilis transposition (stimulated)).

Anal Plug

Previous attempts to occlude the lumen of sigmoid colostomies were abandoned because of pressure necrosis⁴⁵. Mortensen and Humphreys⁴⁶ investigated the efficacy of an expandable anal plug device. The plug is wrapped in a water soluble coat and is inserted like a suppository. The wrapping dissolves after contact with body fluids and the plug expands. The expanded plug sits in the upper portion of the anal canal and can be removed by pulling on the gauze tape which protrudes from the anal canal. The used plugs can be flushed away or disposed of in a similar fashion to a sanitary towel. Nine out of their twelve patients completed the study for

three weeks. The patients used on average eleven anal plugs per week. The plug was in place for a median of twelve hours (range 1-25), with an 82% reported success rate. Three patients found the insertion difficult.

Surgical Correction of Fæcal Incontinence

Where conservative attempts to treat fæcal incontinence fail, surgical correction may be attempted in appropriate patients. The surgical options include muscle repair or supplementation procedures, anal encirclement procedures, fæcal diversion and possibly the insertion of an artificial anal sphincter. At the moment there are only two methods of surgical treatment for fæcal incontinence in which large numbers of patients have been properly assessed over long periods of follow-up, namely sphincter reconstruction and postanal repair. Sphincter reconstruction is reserved in cases of demonstrable trauma to the sphincter ring, whereas postanal repair is usually confined to patients with idiopathic or neurogenic fæcal incontinence, incontinence associated with rectal prolapse or associated with the descending perineum syndrome. The results of surgical correction are summarized briefly in the following paragraphs.

Anorectal muscle repairs

Apposition, Overlapping and Reefing of sphincters

The aim in these procedures is to reconstruct the damaged sphincter as much as possible, and sometimes the choice of the procedure is determined by the extent of the muscle damage and the amount of tissue available for reconstruction after dissection. Overlapping may result in a stronger repair than simple apposition. In a study of anterior sphincteroplasty in a population of 55 women with incontinence due to obstetric or surgical trauma⁴⁷, the authors report a failure rate of 29%.

Reefing, (plication of the deep parts of the external sphincter and puborectalis sling anteriorly or posteriorly) is the operation commonly employed transvaginally for posterior repair of rectocele and occasionally for anovaginal reconstruction following obstetric trauma. Stenosis of the anal canal can be caused if the repair is too tight. As the cause and degree of damage, the timing of the repair and the operation details are hard to standardize, the results and relative merits of each operation cannot easily be compared in the limited studies that are available⁴⁵.

Postanal pelvic floor repair

The late Sir Alan Parks believed that the anorectal angle is of paramount importance in maintaining faecal continence and that the forward pull of the puborectalis sling is the prime mechanism for its creation¹⁵. This mechanism was thought to create a “flap valve” at the top of the anal canal to enhance continence, especially during increases of intraabdominal pressure (for a more detailed discussion of the anorectal angle and the valve theories, see: A Review of the Physiological Faecal Continence Mechanisms, Chapter 1: Does anorectal angle contribute to faecal continence?, Chapter 2: *In-vitro* assessment of the anorectal flutter valve theory).

He developed the operation of postanal repair^{15,48} which was aimed to recreate the anorectal angle without affecting resting anal pressure⁴⁹. It has subsequently been shown that the length of the high pressure zone is increased^{49,50}. An improvement in the resting and voluntary anal pressures has been reported in some studies⁵⁰⁻⁵². In contrast, some studies failed to show improvement of the anorectal angle^{50,52}, or improvement of this parameter compared to controls did not correlate with improvement of faecal incontinence⁴⁹. The long term clinical results of the procedure are disappointing (Table 1).

	Womack et al (1988) ⁴⁹	Yoshioka and Keighley (1989) ¹	Setti-Carraro et al (1994) ²
<i>n</i>	16	124	42
Improved	88%	81%	66%
Fully continent	38%	24%	26%
Follow-up	15 months	3 years	6.2 years

Table 1: Summary of the clinical results of the postanal repair operation.

Perineal muscle supplementation

Gluteus maximus transposition

Sartorius

Vastus medialis transposition

Adductor longus transposition

There is little meaningful data concerning long term functional results and morbidity of these procedures, because the literature, such as it is, essentially consists of papers noting only a few cases⁴⁵. The obvious conceptual advantage of using the gluteus muscle for supplementing the anal sphincter is the fact that contraction will more effectively result in closing of the anal orifice since the muscle normally acts as an accessory sphincter when impedance of elimination is desired. Christiansen et al⁵³ reported their experience with seven patients receiving a bilateral gluteus maximus transposition. Their group consisted of five women with incontinence secondary to trauma and two men with history of anorectal atresia. Three women improved, but the rest were not after one year. There was no change in rectal sensitivity or volume retention tolerance in any of the patients, and only moderate increase in the resting and maximal squeeze pressures was observed in the patients who improved. As with the gracilis muscle transposition, narrowing of the anal orifice may be a factor that contributes to improved function.

Gracilis transposition and electrical stimulation

The transposed Gracilis is the most widely used pedicled muscle graft for the treatment of anal incontinence. The muscle may be transposed unstimulated⁵⁴ or stimulated using an implantable electrical stimulator^{44,55}. Preliminary results of stimulated graciloplasty for the correction of urinary incontinence have also been reported⁵⁶ (two out of the three patients studied achieved urinary control and the third

reportedly improved). Electrical stimulation of the transposed sartorius has also been reported in dogs^{43,57} and the biceps femoris in humans⁵⁸.

Gracilis transposition (non-stimulated)

The gracilis muscle, the most superficial muscle in the medial aspect of the thigh, is broad in the upper thigh, becomes narrow and tapers to a tendon which inserts below the tibial tuberosity. The primary blood supply for this muscle enters proximally, therefore, division at the insertion and mobilization of the muscle to the proximal neurovascular bundle should not compromise viability. This may not be the case as there is a relatively high incidence of ischaemic necrosis of the mobilized muscle. It has been reported that the incidence of ischaemic necrosis can be dramatically reduced by division of the muscle tendon several weeks prior to mobilization to allow rudimentary vessels to open up between the segmental blood supply⁵⁹.

In 1952, Pickrel and associates⁵⁴ developed a procedure using the gracilis as a substitute anal sphincter and reported their experience in four children. Whereas this operation is a useful and effective procedure for selected patients when a supplementary sphincter is required or when multiple attempts at primary repair have failed (e.g. young patients, those who have sustained trauma are those with anorectal malformations), it nevertheless is an esoteric sphincter repair operation to be used only in limited circumstances. The technique is described elsewhere^{45,54}. Variable results are reported, with improved continence ranging from 0-50% and full continence achieved in 0-80% of patients⁵⁹.

Gracilis transposition (stimulated)

Historical and experimental background

Baeten and associates⁶⁰ reported the case of a female patient who had a gracilis sling operation in childhood with a poor result, and subsequently had an

electrical stimulator implanted at the muscle's motor point in adult life. She became fully continent upon stimulation of the gracilis.

Electrostimulation of a muscle using a pulse generator to stimulate its neurovascular bundle will convert fast twitch to slow twitch fibers which have far greater resistance to fatigue⁶¹. This transformation is reversible upon cessation of the stimulation⁶².

A canine model to study the effects of chronic stimulation on a Thiry-Vella loop created by the sartorius muscle was described by Hallan et al⁴³. Stimulation for six to eight weeks at 2-4 Hz resulted in significant reduction of the muscle's fusion frequency (22.2→14.4 Hz). Holdback of liquid at 100 cmH₂O applied to the colonic reservoir proximal to the sphincter was maintained for 1.4 minutes prior to chronic stimulation to 5.6 minutes post stimulation. Histology showed evidence of fibrosis, atrophy and fatty change in parts of the muscle but also evidence of regeneration. This study, however, did not contain unstimulated controls. In a subsequent study of a similar model⁵⁷, each Sartorius muscle was transposed around either end of a Thiry-Vella loop. One muscle was stimulated for eight weeks and the other served as an unstimulated control. Morphological changes of fast to slow twitch fibers were observed in the stimulated muscles. The retention times of liquid at 85 cmH₂O applied proximal to either neosphincter in each loop increased from 10 seconds to 5 minutes. The observed muscle fiber transformation was not essential for increasing the acute retention of liquid in this model. Ideally there should have been morphological data from unstimulated control animals (i.e. animals where neither of the two muscles had been stimulated), especially since relatively high voltages of stimulation were used (voltage increased from 0.75 to 2.75V at the end of the eight week period).

A graciloplasty procedure with investigation of the optimum stimulation parameters was described in the rabbit⁶³. Stimulation for more than six weeks at a frequency of 10 Hz produced satisfactory transformation as evidenced by the

decrease in summation frequency. A similar frequency of stimulation (12 Hz) was used in the Human^{55,59}.

Human studies

Cavina et al⁶⁴ reported good initial results in 47 patients (65% improvement in continence) following short term intermittent external stimulation of the transposed gracilis. They used externally stimulated wires which were removed following the period of stimulation. Such a technique could not have led to conversion from fast twitch to slow twitch muscle.

Williams and associates presented their results of a model for the creation of an anal neosphincter using the transposed, electrically stimulated gracilis muscle in humans^{44,55}. They now use a totally implantable electronic stimulator, the stimulus parameters of which could be programmed and changed using an external programming telemetry transmitter and which could be switched on or off by a patient with the use of a magnet. Basal pressure of the anal canal did not change, but squeeze pressure was enhanced upon stimulation (this was preceded by a transient decrease). Transformation of fast fatiguable to slow non-fatiguable muscle fibers was demonstrated morphologically and histochemically. These changes were reversible as previously reported⁶² if the neosphincter remained unstimulated for more than 180 days. Some atrophy of the transposed muscles is reported in this and other studies^{43,57,64}. Endomysial collagen increased from 4.9 to 7.6% following transposition and stimulation⁵⁷ of the sartorius and the stimulation voltage had to be increased from 0.75 to 2.75 V. These changes are thought to be due to the transposition of the muscle. This effect is observed in humans as well: the voltage to achieve stimulation and palpable contraction of the gracilis neosphincter increases with time⁶⁵.

The operation of electrically stimulated graciloplasty is described in detail by Williams⁵⁹. They report the construction of an electrically stimulated neosphincter in 23 patients with faecal incontinence as well as ten patients as part of a total

reconstruction after abdominoperineal resection of the rectum. The patients selected for this procedure were those in whom a conventional operation to correct their incontinence had either failed or was contraindicated and in whom a colostomy was the only other option. Sixteen of the patients with incontinence are reported to have functioning neosphincters, all of whom have improved and most have “acceptable”, though not perfect continence.

A new modification to this procedure using both gracilis muscles has been reported⁶⁶. Instead of fixing the gracilis tendon to the ischial tuberosity, both gracilis are mobilized and wrapped around the anal canal and their tendons are fixed to one another. This guarantees the presence of a greater muscle bulk and also possibly enhancing the anorectal angle. The authors report a 90% success rate in a heterogeneous group of ten patients (mainly related to trauma to the sphincter or congenital conditions) with concomitant increase of resting and maximal squeeze anal pressures.

Contraindications of electrically stimulated gracilloplasty

1. Damaged gracilis muscle. If there is any doubt about gracilis muscle function, this should be tested by electromyography. In practice, this includes patients with spina bifida and those with generalized neurological or myopathic disorders (e.g. patients with multiple sclerosis or myopathic diseases affecting the limb muscles). Mechanical damage or absence of the muscle may not be a contraindication as in some cases the biceps femoris may be suitable⁵⁸.
2. Disseminated malignant disease or local pelvic recurrence.
3. Lack of sufficient manual dexterity to use magnet controls of the electrical stimulator.
4. Persistent perineal sepsis or Crohn's disease.
5. A cardiac pacemaker *in situ*.

This technique, although promising is still in its infancy. It may, however, become the optimum method of muscle transposition in the future.

Anal encirclement procedures

Thiersch operation

The original description of anal encircling procedures was advocated for the management of rectal prolapse, but various materials have been implanted around the anal canal in an attempt to enhance continence. These were: silver wire, merselene, silastic ribbon or a Dacron impregnated silastic strip. The technique has also been reported in an canine ileostomy model⁶⁷. The main complications included infection, erosion, persistent incontinence, faecal impaction, development of anal stricture and pain. Corman⁴⁵ reports a 65% success rate in 38 patients.

Fascia lata

Encircling the anal canal by a fascia lata sling was first reported by Stone in 1924⁴⁵. Fascia lata may be associated with less of the complications relating to the presence of foreign material around the anal canal.

Anal encircling procedures suffer the limitation of creating a non adjustable stenosis (albeit relative) of the anal canal which has a significant chance of being either too narrow or too wide, who's reversal may, in some instances, be impossible.

Colostomy

Only rarely should colostomy be considered the preferred recourse in the management of patients with faecal incontinence. The performance of a colostomy in a patient with faecal incontinence is thought generally to be an admission of failure, but it should not be regarded as such. Many individuals should be spared the ardours and pain of futile attempts to perform esoteric reconstructive procedures when the likelihood of success is extremely limited. Patients with severe neurological

dysfunction, major trauma or congenital absence of the perineal musculature may be happier with the formation of a well sited colostomy than an incontinent perineal colonic termination. Perhaps more frequently than in any other condition, those with faecal incontinence need to be willing partners in the decision making process.

Artificial anal sphincter prostheses

A small but significant proportion of patients will remain helpless despite exhaustive attempts to improve their continence mechanism. Some of these patients may benefit from the insertion of an artificial anal sphincter.

The previous attempts to design and implant an artificial anal sphincter in animals and humans are reviewed in the next chapter (Attempts to achieve continence artificially: A Review).

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Attempts to achieve continence artificially: A Review

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Introduction

Incontinence is underreported, underestimated, represents an enormous social and psychological problem and the current results of its management are poor. The results of surgical correction for faecal incontinence are reviewed in the previous chapter. For those patients whose incontinence failed to respond to conventional means, there is little to offer except the implantation of an artificial sphincter. The history and evolution of the devices designed to attempt to achieve continence of urine and faeces are reviewed in this chapter.

Artificial devices for the treatment of urinary incontinence

Urinary incontinence is by itself a socially disabling condition. Many methods of treatment have been tried in the past, including penile clamps^{1,2}, external collecting devices, indwelling catheters, surgery to increase the resistance of the bladder neck and urethra, electrical stimulation^{3,4} and suprapubic urinary diversion^{5,6}, but none is ideal⁶. Penile clamps and external continence devices are cumbersome and non-physiologic. Indwelling catheters can become encrusted and lead to recurrent urinary tract infections. Surgery on the bladder neck and urethra may permanently increase the resistance, with the result that in some cases the patient can empty the bladder only through intermittent catheterisation. Patients with urinary diversion have a stoma and possibly an external collecting device or depend on intermittent catheterisation.

The early designs

The idea of creating an artificial sphincter for control of urinary incontinence is not new. Foley (also the inventor of the catheter that bears his name), reported a device in 1947 that resembled a sphygmomanometer^{1,2}. It consisted of an inflatable cuff that was placed around the anterior urethra in a tunnel lined by skin, and a detachable pump that was carried in the patient's pocket and was connected to the cuff by rubber tubing. This device was only suitable for male patients. To void, the

user deflated the cuff. After the bladder had emptied, the patient inflated the cuff to compress the urethra and become continent again. This artificial sphincter had two main design defects: it was an external device, as inert materials were not available at that time, and it had no mechanism for limiting the compression of the urethra. The pressure applied frequently rose above arterial pressure causing ischaemia and necrosis of the urethra. Therefore, it was never a practical apparatus and was soon abandoned.

In 1973, Kaufman reported the implantation of a rectangular shaped silicone gel prosthesis at the base of the bulbar urethra⁷. This produced permanent increase in the urethral pressure and caused a relative stenosis (cf. Thiersch operation or Angelchick prosthesis, apart from the fact that this prosthesis was non-encircling). This device never gained popularity despite the preliminary reports of short term success⁷⁻⁹ and a reported success rate of 55% in 57 patients with post prostatectomy urinary incontinence¹⁰.

In 1974, Giori disclosed the patent of a semi-passive implantable urethral occluder⁷ (Figure 1).

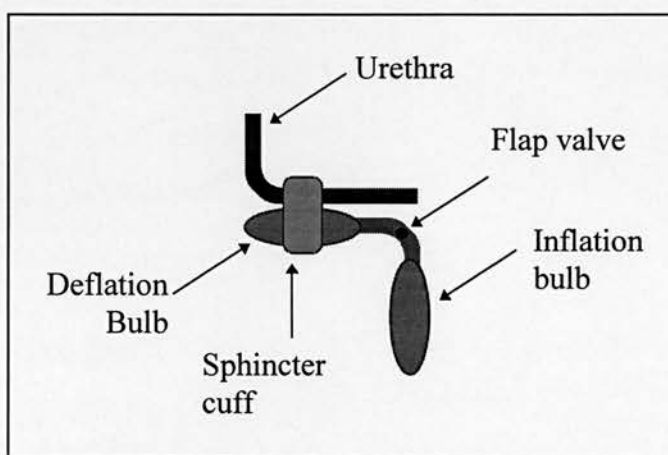


Figure 1: The Giori patent⁷. Pressure on the inflation bulb occludes the urethra. Pressure on the perineum squeezes fluid out of the deflation bulb, allowing micturition to occur.

The device was implanted through a perineal incision and operated by manual pressure on the perineum: pressure on the inflation bulb forces fluid into the sphincter end of the prosthesis, where the surrounding cuff or ring occludes the urethra. Pressure on the cuff forces fluid through the flap valve to open the urethra.

The above design is reported to have been used “successfully” in a series of unpublished trials¹¹. It is not in clinical use in so far as can be determined.

The first devices which would open and close the urethra at will were reported in 1973¹²⁻¹⁵. Summers¹², patented a device whereby a cuff occludes the urethra by reversible filling from a balloon reservoir. This appears to be a volume set device with a magnetically operated valve. No evidence that this device has been tested *in-vivo* could be found.

The device invented by Buuck¹³ (original patent filed in 1973 and subsequently called the AMS 721) was the first of a family of artificial sphincter devices patented and produced by American Medical Systems (AMS). These devices will be discussed in detail in the next section of this chapter, as they remained the only clinically (and commercially) viable implantable artificial sphincters.

Rosen described a prosthesis to occlude the urethra¹⁶⁻¹⁹ in 1975. This prosthesis is only suitable for male patients. The device is composed of a three-pronged clamp, two arms of which are parallel one on each side and a single, central arm carrying a cylindrical balloon opposing them (Figure 2). These arms fit transversely across the urethra. The balloon is connected via reinforced tubing to a reservoir bulb containing isotonic saline and a release valve. Compression of the bulb inflates the balloon elevating and compressing the urethra to achieve continence. Voiding is allowed to occur on deflating the balloon by pressing the release valve. The author presents 16 patients, with satisfactory results in ten (an extra four patients are mentioned anecdotally with “excellent outcome”). Maximum follow-up was for two years. The device was not set to apply a predetermined pressure on the tissues and presumably this was set empirically. The inside edges of

the fixed prongs could cause localized high pressure application points on the tissues, which would lead to necrosis and urethral erosion. This is also complicated by the fact that there is no relief valve to maintain a constant safe pressure on the urethra, nor a mechanism to dissipate potential high pressure transients in the system and prevent them from being applied on to the tissues.

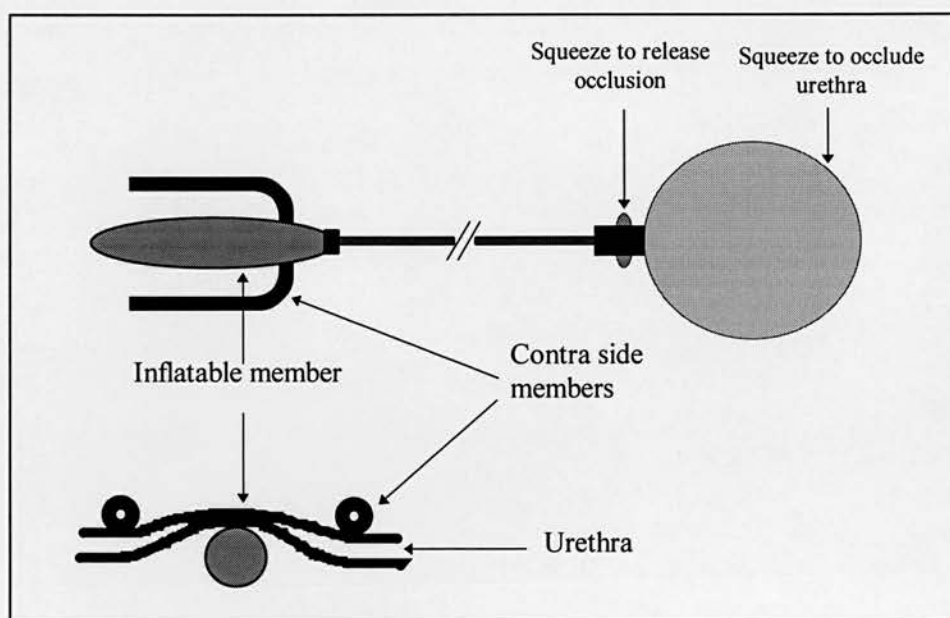


Figure 2: The artificial urethral sphincter described by Rosen¹⁷.

In summary, this sphincter is based on the Foley device, but is fully implantable. By being a volume dependent system, however, it suffers from the inherent deficiency that the pressure within the urethral occluder is neither controlled nor monitored. Volume controlled sphincters have had a poor success rate and have not gained favour with many urological surgeons. This device, therefore, remains of historical interest only.

A magnetically operated device with the magnet placed in the vagina was assessed in merino sheep²⁰ and produced no ischaemia for up to 33 weeks. The device was used in two patients²¹ but there are no other reports describing its clinical use.

The AMS family of sphincters:

AMS 721, AMS 761, AMS 742(A, B, C), AMS 792, AMS 800

These devices were described in a series of patents^{13,22-25}, produced commercially and implanted in a large number of patients. The currently available device is the AMS 800. A review of the results of the implantation of this device and an analysis of 4130 complications reported to the FDA are analyzed in the following chapter. A summary description of each device appears in Table 1.

Early collaboration between the medical device industry and NASA was critical to the success of this effort to reduce patient risk and health care costs by the incorporation of high reliability aerospace components in this new prosthesis. To ensure availability of the NASA technology to the entire medical community, NASA's methodology emphasizes projects that lead to the development of commercially available medical products incorporating NASA technology. The development of this improved artificial sphincter is an example of a successful transfer of aerospace technology to medicine²⁶.

Detailed analysis of the engineering drawings and operation of the devices is described in Appendix 3.

Model	Mechanism	Special Features	Year Filed	Ref.
AMS 721	Inflate bulb (R side) Deflate bulb (L side)	Pressure regulated by mechanical valve (V4). Balloon does not regulate pressure.	1973	13
AMS 761	Inflate bulb (R side) Deflate bulb (L side)	Pressure Regulating Balloon Reservoir (PRBR). Valve (V4) still present. Only assessed for short period. Superseded.		27
AMS 742	Single deflate bulb (scrotum or labium)	PRBR. Refilling time controllable by variable resistor. (A, B, C models described in the text)	1977	22
AMS 791, AMS 792	Single deflate bulb (scrotum or labium)	PRBR. Single control assembly contains resistor and one way valves. System must be surgically activated for the first time after implantation.	1977, 1989	22,23
	As AMS 792 but incorporating a coil, remotely controlled.	Induction coil incorporated in the design to open the cuff when inductively heated transrectally. Not clinically viable.	1989	23
	Single control valve, incorporating balloon in same assembly	Magnetic activation/deactivation valve. Volume controlled device, with balloon incorporated onto pump case. No pressure regulation. Not used clinically.	1990	24
AMS 800	Single deflate bulb (scrotum or labium)	As AMS 792, but control pump assembly incorporates a shutoff valve for long term deactivation. Can be left primed at implantation and activated non surgically.	1984	25

Table 1: Summary of the features of the AMS sphincters.

The idea of the pressure regulating balloon reservoir was included early in the design process²². A silicone balloon with a sigmoid pressure-volume relationship is incorporated (Figure 3). The pressure increases upon inflation up to a plateau level and this ensures that the system pressure does not exceed a maximum level which is

considered safe when applied on to the tissues. By using balloons of different wall thickness, the level of the plateau can be varied.

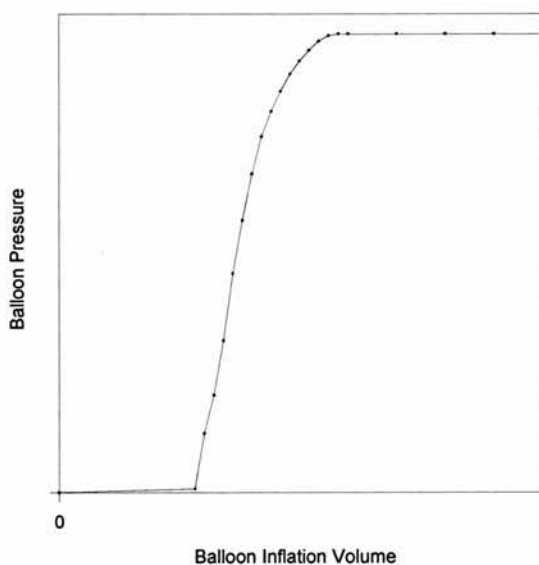


Figure 3: Pressure volume relationship of a typical pressure regulating balloon.

It is possible for the sphincter to be set to operate at a pressure level slightly lower than the plateau pressure and this would have the added advantage that the operating pressure can be varied by subsequently injecting fluid in the system without the necessity to surgically replace the balloon (this is the method used by the author - see Chapter 6).

The AMS 721

This was the original device released by AMS¹³ (Figure 4). Its operation was assessed in eight mongrel dogs for up to six months and inflation periods of up to 12 hours²⁸. Satisfactory continence does not appear to have been achieved and the description of the rest of the results is sketchy and weak scientifically. Nevertheless, this device was implanted in humans and was in use for approximately three years. It was very difficult to implant due to the large number of components which necessitated extensive tunneling and dissection. A pressure regulating balloon reservoir was incorporated in a subsequent modification of the device (AMS 761) in order to overcome the problem of high pressure being applied to the urethra by overdistension of the reservoir or other possible malfunction. It also became obvious that the complexity of the design and the critical central rôle of a collection of spring loaded valves of different characteristics were contributing to an increased number of complications and this device was being rejected both by patients and clinicians. This rapidly led to a complete redesign of the device and the AMS 742 was introduced²².

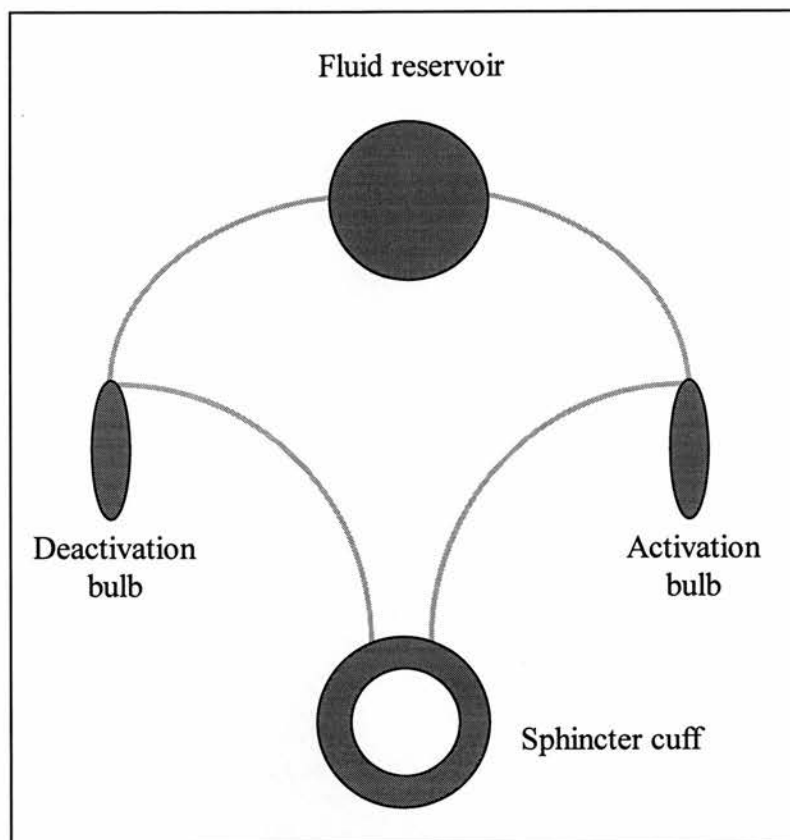


Figure 4: The AMS 721. The bulbs are implanted subcutaneously and the reservoir intraperitoneally. The position of the one way valves is not shown.

The AMS 742A and AMS 742, 742B, 742C²²

The evolution of this device (Figure 5, Figure 6) was necessary to minimize the components that had to be implanted in order to make implantation more straightforward, make it more convenient for the patient to operate and reduce the number of malfunctions associated with the multiple valves in its predecessors (AMS 721/761).

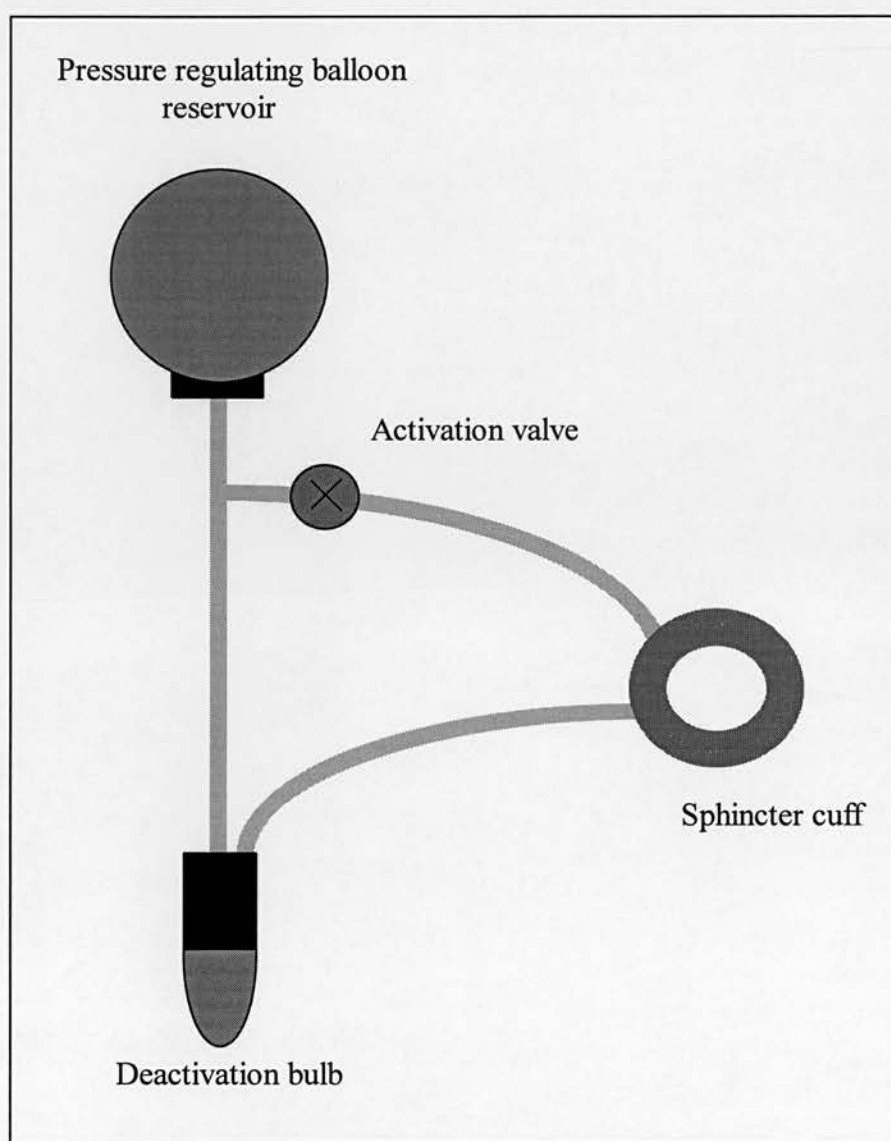


Figure 5: AMS 742A. This device was quickly superseded by The AMS 742 which was simpler and easier to implant and operate.

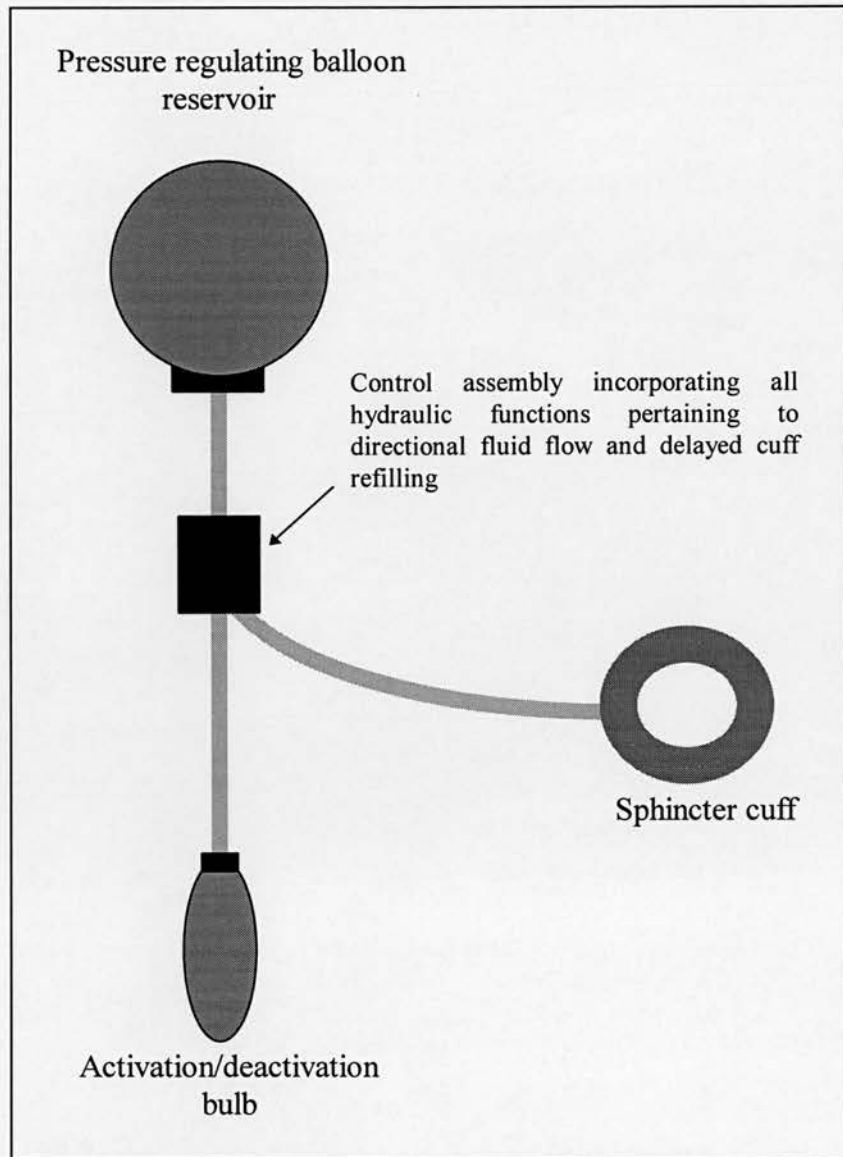


Figure 6: The AMS 742²².

The design of the cuff and control block assembly provides for two models: the 742B and 742C. The B model is used for ease of tubing connection with urethral cuff placement and the C control assembly is used for ease of tubing connection with vesical neck cuff placement.

In one study²⁹, a total of 47 patients (41 male and 6 female) had implantation of the AMS 742. Of the 42 patients who had primary activation 34 experienced continence without further surgical revision. The remaining five patients who primarily had deactivated devices subsequently had the devices activated and the patients were dry. Of the eight patients with initial failures two had infection and six had primary cuff erosion of the urethra. In four of the eight patients the cuff was replaced, and the device was deactivated and then activated after three to four months. All four of these patients were continent. Follow-up for these patients ranged from 6 to 30 months. Overall, 43 of the 47 patients were continent (90%).

Compared to the previous model this simplified design provides for much easier implantation, more reliable function related to cuff pressures and to cuff configuration, and more flexibility in the selection of the site for cuff placement. In addition, this new device has enabled the development and use of a new concept of primary and secondary activation. Delayed activation allowed tissue healing to occur in four cases where the cuff was revised²⁹ and represents an added advantage to the design.

Other patented but untried devices

The patents filed by AMS are quite broad and include some interesting ideas that have not been applied clinically. They were almost certainly included in order that full commercial protection against minor patent modifications could be afforded.

The Burton patent²², includes another two designs in addition to the AMS 742: it describes a device with a double balloon reservoir and a manual deactivation valve which, when depressed, would empty the cuff by transferring fluid between the two reservoirs. This device has not been produced commercially to the knowledge of the author. A minor modification to strengthen the anchoring of the cuff is also described. The other device described is essentially the AMS 792. The slow leakage re-equilibration pathway (a resistor made from porous glass material) is first described in this patent.

Polyak²³ describes a modification of the above, whereby a heating coil is incorporated in the cuff mechanism. Another coil is inserted into the rectum and it inductively heats up the coil in the cuff. The theory is that the heated coil will deform and open the cuff. Perhaps not surprisingly, this device has neither been produced commercially, nor been tried in a clinical setting. In a subsequent patent ²⁴, Polyak discloses another mechanism, whereby both the pump and reservoir components are incorporated into one assembly resembling that of an artificial penile prosthesis³⁰. This design would be quite bulky and would not compensate for increases in intra-abdominal pressure. It was not developed further. In the same patent, a magnetically operated deactivation valve incorporated in the control pump is disclosed. Once again, there is no evidence that this has been used in a clinical setting.

The AMS 800

This is the currently available device. It was introduced in 1980 by Burton²² and patented in its current form in 1984²⁵ (Figure 7). A detailed review of the engineering drawings and design features of the device is presented in Appendix 3.

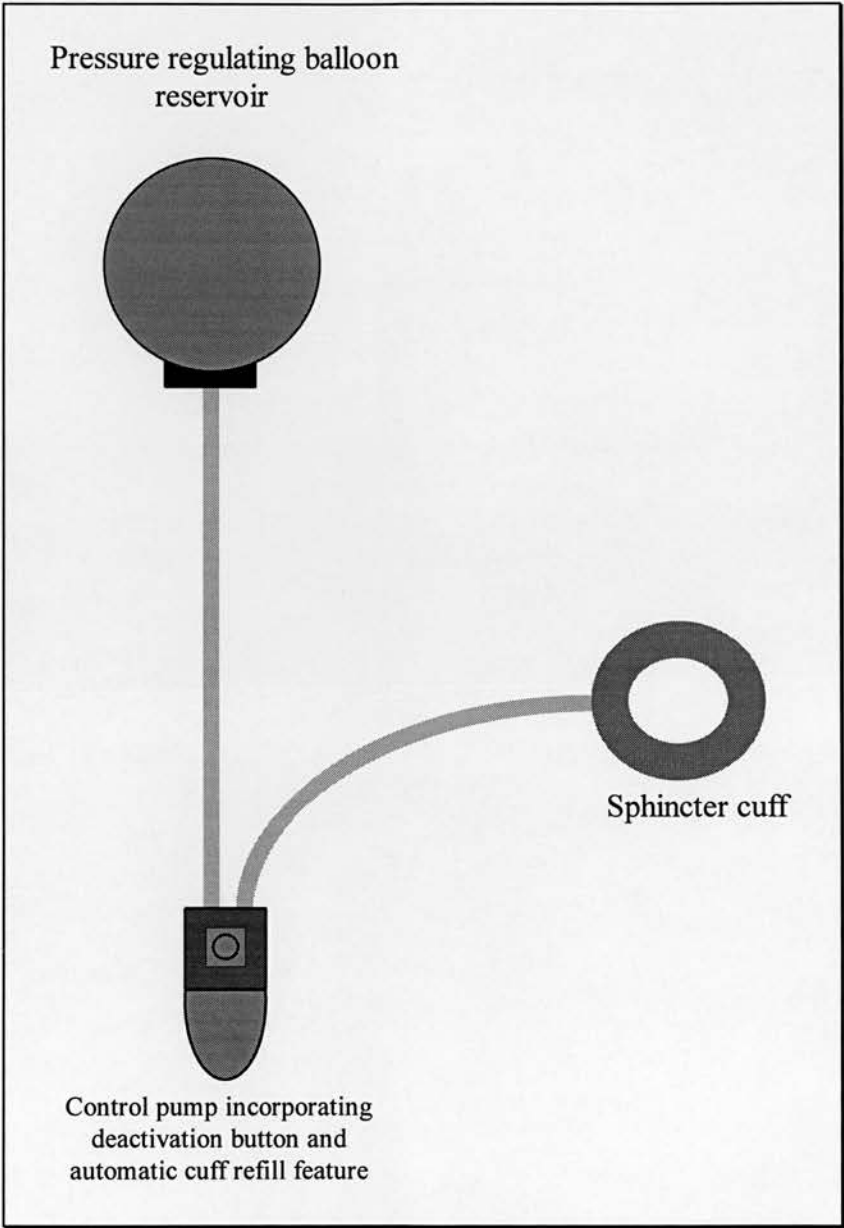


Figure 7: The AMS 800 artificial urethral sphincter. The control mechanism incorporates an automatic re-equilibration feature and a long term deactivation mechanical valve.

The AMS 800 sphincter involves several modifications to the control valve that simplify its implantation and operation by the patient. The device is implanted using the chosen size of cuff around the urethra and a reservoir of the appropriate plateau pressure (these are currently available with plateau of 51-60, 61-70 or 71-80 cmH₂O). The device is suitable for both males and females (the pump is implanted in the scrotum or the labium as appropriate). It is implanted fully primed with radio-opaque fluid in its deactivated state (cuff empty and deactivation button engaged). After approximately three to six weeks to allow for tissue healing, the device is activated for the first time by sharply squeezing the bulb. The cuff closes in approximately three to five minutes. Further pumping of the bulb moves fluid into the reservoir and empties the cuff, thus opening the urethra. The cuff closes automatically once again after several minutes, when micturition is complete. The unit can be deactivated by pressing the deactivation button on the pump before refilling of the cuff commences. One must ensure, however, that the bulb always remains full as one pumping stroke must always remain available to allow subsequent re-activation.

This device has been implanted in an estimated seventeen thousand patients worldwide. A review of its complications is presented in the following chapter.

The AMS 800 around bowel in urology³¹⁻⁴³

Reconstruction of the urinary tract after diversion has been successful in patients with normal innervation of the lower tracts. However, the possibility of urinary incontinence after such major surgical procedures has dissuaded many surgeons from attempting urinary undiversion in patients in whom the continence status cannot be determined accurately before the operation or who were known to be incontinent before the original diversion. Light, Flores and Scott³¹ first reported the implantation of the AMS 792 around the bowel neourethra of a patient with urinary undiversion in 1983 and they reported on two further patients shortly afterwards³². The potential use of the artificial sphincter around bowel extended the versatility of

the device and offered many possibilities for reconstructive procedures involving bowel.

Most of our understanding of the effects of the AMS 800 sphincter on bowel is based on animal^{35,44,45} and human studies³⁵ by Engelmann and his co-workers. The device was assessed by implantation around isolated intestinal loops in New Zealand rabbits. Twenty two animals are reported in the first study⁴⁴ and 40 in subsequent reports^{35,45}. Ten animals were sham operated and six acted as controls. The evaluation included the effect of varying closing pressures of the cuff on the cuff six weeks after implantation. This was assessed macroscopically, by microangiography and histologically. The sphincter was able to achieve continence during perfusion of the intestinal loop, holdback pressures being dependent on the cuff pressure. 60 to 80% of cuff pressure was transmitted on to the bowel. Atrophy was present to some degree at all sphincter pressures. Mucosal ulceration was noted at cuff pressures above 80 cmH₂O. Microangiography showed rarefaction of mucosal blood supply and neovascularisation at the level of the fibrous sheath and the cuff border. Sphincter related complications (cuff erosion and atrophy) were pressure dependent and seen mainly in high pressure groups (Table 2).

Total number	Pressure (cmH ₂ O)	Sphincter related complications	
		Number	%
6	0	1	17
4	40	1	25
5	60	2	40
7	80	2	28
4	100	4	100

Table 2: Sphincter related complications were pressure dependent in rabbit intestinal loops⁴⁵.

Other consistent changes were the development of a fibrous sheath around the bowel beneath the cuff and the cuff itself and fibrous peritoneal reaction and intestinal adhesions at the cuff site.

Similar results were reported in 24 dogs with a Koch's pouch³⁵. The device was activated twice per day for up to 29 weeks. There was no erosion of the device at cuff pressures less than 80 cmH₂O and this was taken to be the maximum safe pressure that can be applied on to the bowel.

Protection of the bowel wall may be afforded by interposing omentum³⁶ or a rectus muscle flap⁴³ between the sphincter cuff and the wall of the bowel. This may act as a cushion to dissipate some of the applied pressure and also to protect the bowel from crenation³⁷ into the high pressure areas inside the cuff folds. In addition, it may provide an improved blood supply.

The features and trouble-shooting of the device are reviewed by Light³⁴ who also presented their experience with implantation of the device around the ileum in augmentation ileo(caeco)plasties in 14 patients (Light and Engelmann³³). The main

complication appeared to be incontinence due to unpredictable bowel contractions causing increases in intra-vesical pressure. Long term results are available in four of these patients³⁷. Various components of the sphincter were revised at least seven times over an eleven year period in one patient. Atrophy and erosion occurred at a cuff pressure of 80 cmH₂O in this patient. In the second patient, following several complications, a 51-60 cmH₂O balloon was inserted and the device was working satisfactorily at 6.5 years. In the third patient the device was working well at a cuff pressure of 61-70 cmH₂O after 3.5 years. In the fourth patient, multiple complications related to atrophy and infection and a continent diversion was eventually performed. Implantation of the device in association with the LeBag technique in two female patients was successful in one. The other died six weeks post-operatively of unrelated reasons³⁹.

Mitrofanoff recommends implantation of the artificial sphincter as a means to achieve continence in a failed continent diversion procedure⁴⁶. In their study of two females (follow-up 20 and 32 months respectively) they did not use the standard control pump, but an injection port and a balloon. By implantation in a retroperitoneal position, the balloon lost its pressure regulating capacity and acted as a variable pressure compartment allowing accurate determination of the closing pressure by injecting or withdrawing specific volumes of fluid.

Seven cases of implantation of the device in neobladder procedures have been reported by Grise et al⁴¹. Satisfactory continence was achieved in four cases (follow-up 3-36 months). Burbige reports such placement in nine patients 15 to 28 years old³⁶. A total of 15 complications was experienced in eight patients and 13 secondary procedures were necessary. Follow-up ranged from two to four years. The most common complication encountered was atrophy of the bowel wall deep to the cuff, which was heralded by a gradual onset of stress urinary incontinence that progressed to continuous leakage in eight patients 6-10 months post-operatively. All eight patients underwent successful replacement with a smaller cuff. Another patient continued to have night-time enuresis. The patient in whom an omental wrap was

interposed between the cuff and the bowel wall did not require replacement, but the follow-up time was not reported in this patient.

The Craggs artificial sphincter control pump design

More recently, Craggs presented⁴⁷ and patented a newly designed system initially claiming to have overcome the mechanical problems associated with mechanical control devices^{48,49} (Figure 8).

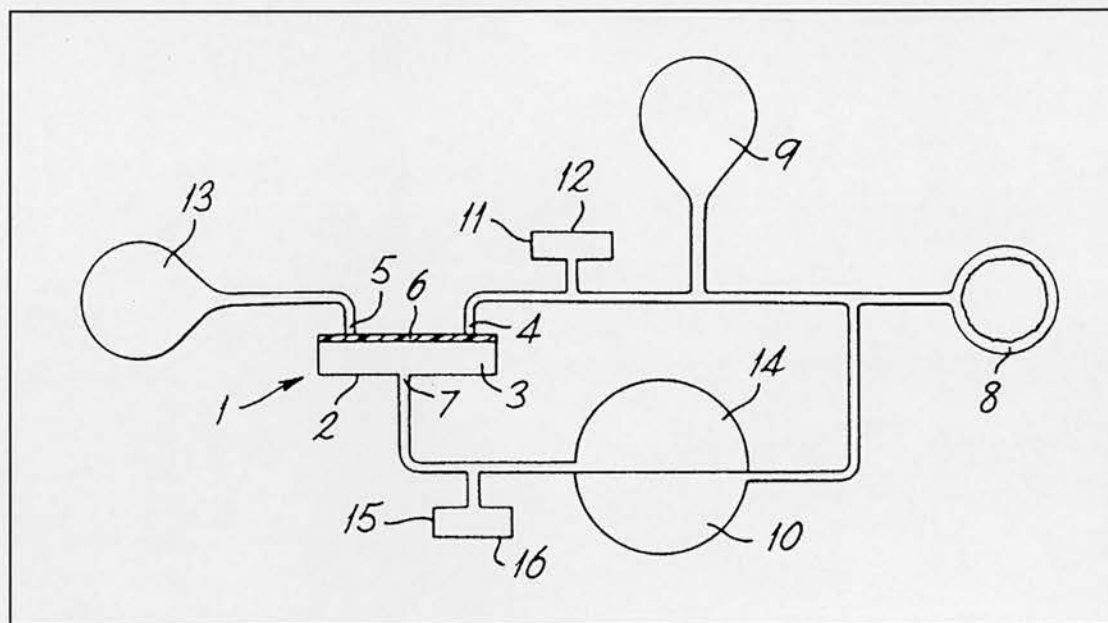


Figure 8: The original design of Craggs⁴⁸.

It comprises a fluid filled reservoir (10), a control mechanism (1), an inflation bulb (13), a deflation bulb (9) and a cuff which is placed around the urethra (8). A preset pressure is theoretically applied onto the tissues and this is controlled by injecting or withdrawing (11, 15) fluid from two self sealing compartments (12, 16). Analysis of the fluid pathways in the patent document is not entirely clear, but the device is designed to maintain tonic occlusion of the urethra, the pressure being exerted by the balloon (14, 10). The same pressure is applied on a leaf “valve” mechanism (6) which is maintained in the closed position until unseated by operation of bulbs 9 or 13. Operation of bulb 13 is supposed to lift the valve and allow fluid *at high pressure* to inflate the sphincter. Operation of bulb 9 is supposed to allow

equilibration to a non-activated state. The author of this thesis cannot see how this could be possible, as squeezing on bulb 9 would develop the same level of high pressure as that in bulb 13. Perhaps it is not surprising that the clinical results have been totally unsatisfactory, with an almost 100% failure rate⁵⁰.

The control pump was redesigned in a subsequent design⁵¹, but is too complicated to show any clinical promise (see analysis of the engineering drawings in Appendix 3). The new pump (12) and an anti-stress incontinence feature (13) have been combined in the latest version^{51,52} (Figure 9).

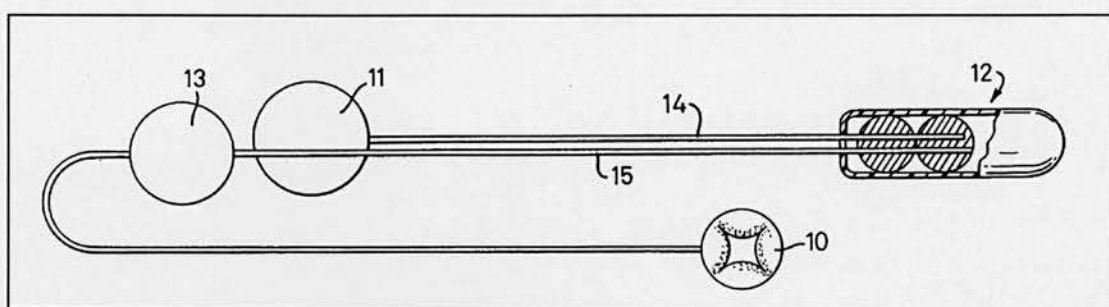


Figure 9: The latest design by Craggs^{51,52}.

The anti-stress incontinence balloon is placed in the peritoneal cavity, so that intra-abdominal pressure changes are reflected onto the cuff pressure. This has been shown to occur experimentally in an *in-vitro* model⁵⁰.

Another weakness of his design is the fact that a “relief valve” mechanism is not incorporated. In the AMS 800 design, the maximum pressure that can be applied on the tissues is determined by the plateau level of the balloon reservoir. In that device, the pressure is truly regulated so that it cannot increase beyond a maximum value. In addition, the way the term “regulated” is used in the description of the Craggs device⁵⁰ is wrong. The pressure in that device is regulated in the sense that it can be adjusted or varied, but is not limited and could increase to dangerous levels quite readily if there is any malfunction.

This device and its modifications are unlikely to prove clinically useful for the above reasons.

The Cleveland Clinic design⁵³

A magnetically activated sphincter prosthesis has been designed to overcome the difficulties encountered with the AMS 800 sphincter by patients with poor manual dexterity (Figure 10).

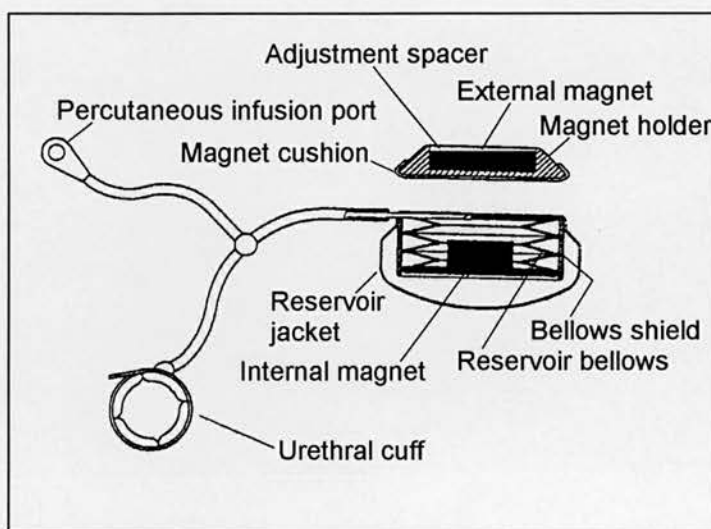


Figure 10: The magnetically activated sphincter prosthesis reported by Fukumura et al⁵³.

The device operation is controlled by an external magnet. When the external magnet is in place, the metal bellows of the reservoir are compressed and the sphincter cuff is closed. Removal of the external magnet from the skin over the implant allows the bellows to expand, thus opening the sphincter. The applied pressure is varied by injecting or withdrawing fluid from the system via an injection port and choosing a magnet of different strength. The effects of this device on skin blood flow has been tested on minipigs⁵³. The pressure applied to the skin was reportedly set to either 10 or 20 mmHg, but the authors do not report how this was measured. Blood flow decreased significantly at 20 mmHg and skin ulceration was

caused in all five experimental animals. One animal in four suffered pressure necrosis to the skin at 10 mmHg.

This device has the following disadvantages:

1. It “defaults” to the activated position if there is a problem with the magnet, or if the patient loses the magnet. Bladder outlet obstruction is, therefore, a real possibility.
2. The strength of magnets decays naturally with time and deactivation of the device may become impossible at an unpredictable point.
3. This is a volume set device and, as already discussed, this may be associated with ischaemic complications as tissue pressure can rise uncontrollably in the absence of a pressure regulating/relief mechanism.
4. The patient may experience complications if an MRI scan is needed.

In conclusion, this device appears to have increased the number of potential ischaemic complications when compared with the AMS prosthesis. For the above reasons, the author of this thesis believes that it has no place in the treatment of incontinence.

Artificial devices for the treatment of faecal incontinence

Attempts have also been made to develop a mechanical prosthetic anal sphincter⁵⁴⁻⁵⁷ but to date these have suffered from many complications. The methods used to occlude bowel (anus or stoma) can be classified as follows:

1. Methods that use external occluding devices:
 - a) Deformable button⁵⁸
 - b) Fluid filled device with surface cover^{59,60}
 - c) Balloon catheter⁶¹
 - d) Magnetically secured devices^{54,62-66}
 - e) Disposable anal plugs⁶⁷
2. Implantation of other valves:
 - a) Porcine aortic valve⁶⁸
 - b) Transposition of the pylorus⁶⁹
3. Methods that use implantable active devices (prosthetic sphincters):
 - a) The Summers¹², Giori⁷ and Rosen¹⁶ sphincters
 - b) The AMS 721 in a canine ileostomy model⁷⁰
 - c) The AMS 721 in a minipig colostomy model⁷¹
 - d) The Haber patent⁷²
 - e) The AMS 800 as an anal sphincter^{41,73-75}
 - f) The AASP 2000 Glasgow Neosphincter⁷⁶

Methods that use external occluding devices

Deformable button⁵⁸

In 1952, a patent was granted to Surface for a colostomy control button⁵⁸ (Figure 11). The device consisted of a hollow gum rubber plug and an aluminium face plate. An introducer stretches the device to allow insertion. The device then returns to its original shape and occludes the lumen of the bowel. It was available in a range of lengths and diameters and was accepted by the American Medical Association's Council on Physical medicine and Rehabilitation⁷⁷. This device was marketed but there was concern about it being used inappropriately by some patients without supervision so the effort was allowed to lapse. There is an anecdotal report that the device had been used successfully by one patient for 22 years¹¹.

With current knowledge and development of silicone elastomers and biomaterials, it is reasonable to conclude that the "Surface" control button could stand re-evaluation.

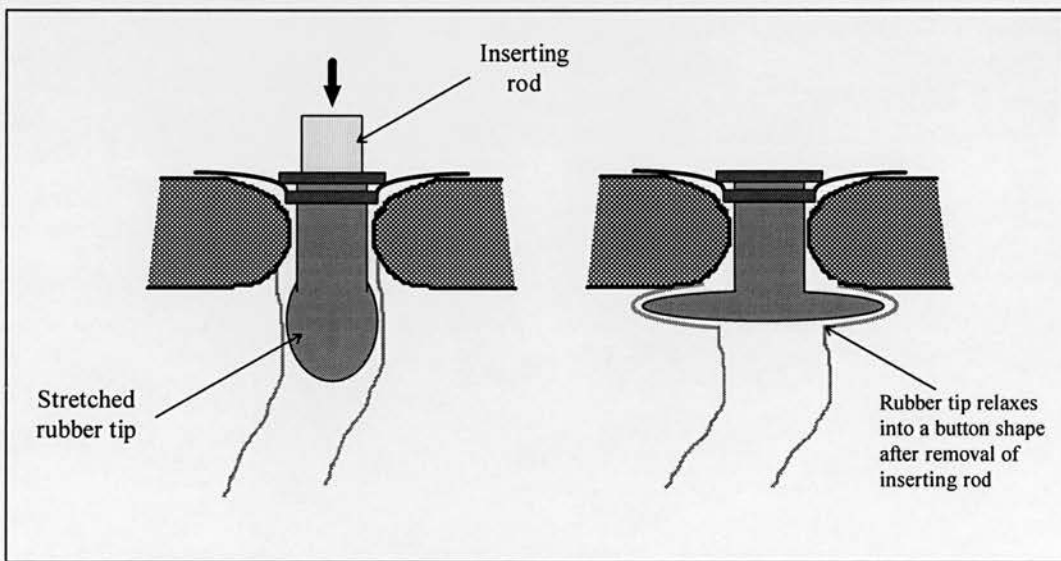


Figure 11: The Surface deformable button⁵⁸.

Fluid filled device with surface cover^{59,60}

Based on the successful use of a fluid filled occlusive device similar to the above in patients with failed continent ileostomy valves⁵⁹, Pemberton and co-workers evaluated extending the use of this device to conventional ileostomies without reservoirs in a canine model⁶⁰. The occlusion period was increased gradually from two to six hours a day and animals were studied over periods ranging from 18 to 22 weeks. All four animals tolerated complete occlusion of up to six hours a day and were continent during that period. There was evidence of proximal dilatation of the ileum acting as a reservoir. This approach has led to the development of a commercially available device (Continent Ileostomy Valve®, Model 236, Waters Instruments Inc., Rochester, Minnesota).

Balloon catheter⁶¹

This simple method involves the use of a Foley type catheter to occlude the lumen of the ileostomy. The catheter was kept in place by applying traction and fixing it on a surface faceplate. Nine piglets were studied (five with a constructed reservoir and four without) for six weeks. Occlusion periods were gradually increased from three to eight hours. All animals were continent during the occlusion periods and there was no morphological evidence of bowel damage. Proximal accommodation increased more markedly in the animals with the reservoir.

Magnetically secured devices^{54,62-64}

Willital reports the implantation of a magnetic prosthesis to occlude the bowel (Figure 12). The implant consists of two halves of a samarium cobalt ring which are positioned around the upper anal canal through a sacral approach without opening the bowel. Occlusion of the bowel is achieved by a special anal tampon/plug made of polyformalvinyl foam which incorporates another magnet. The tampon is stabilized inside the lumen by means of the magnetic attraction force between the two elements of the device. The tampon is changed twice a day.

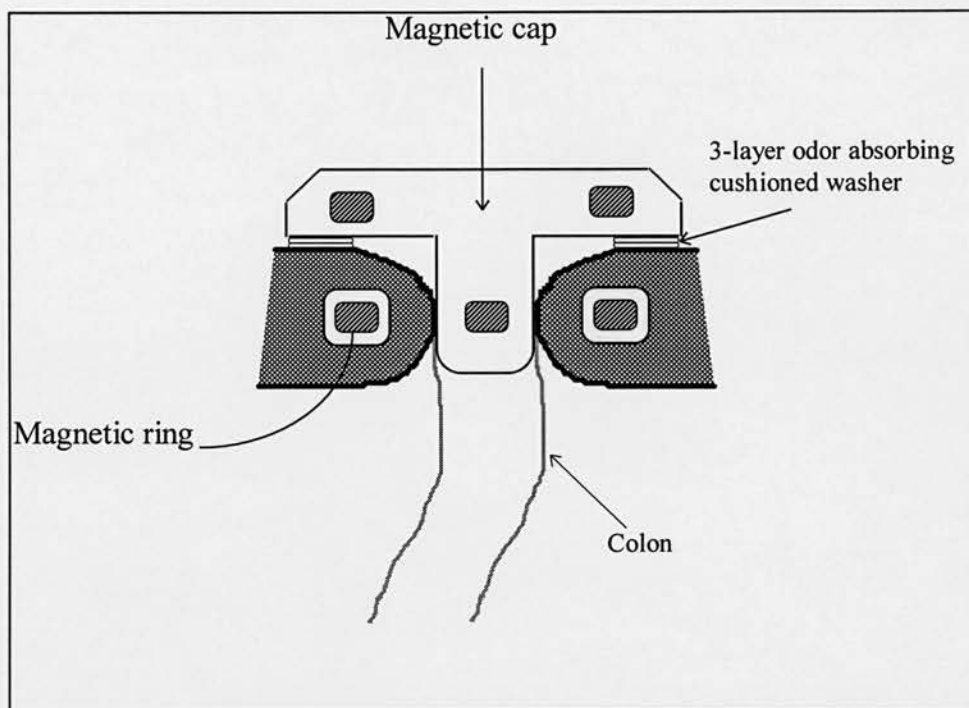


Figure 12: The magnetically secured anal plug⁵⁴.

Six children (age range 3-15 years) with anorectal malformations were implanted with the device⁶³. Complete continence with no complications was reported in the short term, but the device suffered many infective complications and eventual erosion and was not developed any further, despite two further anecdotal reports attesting to its short term success in adults⁶² and children⁶⁴.

Disposable anal plugs

The results of this study⁶⁷ are summarized in the previous chapter.

Implantation of other valves:

Porcine aortic valve⁶⁸

A porcine aortic prosthesis acting as a one way valve was implanted in a canine ileostomy model. The bowel was emptied by intermittent catheterisation. The animals were continent for the eight week study period.

It is obvious that emptying can only be achieved if the bowel contents are liquid. This preliminary study does not address the long term effects of the ileal contents on the biomaterials or the response of the valve cusps to repeated intubation.

Transposition of the pylorus⁶⁹

Transposition of the pylorus to control an ileostomy was performed in six mongrel dogs⁶⁹. Four animals were used as controls. The study animals were terminated at 1, 2, 3 and 7 months. The effluent in the first group was described as paste like, whereas in the control group it was liquid. All control animals died within nine days despite fluid replacement.

Even though this study shows an apparent decrease in transit time, this should be balanced with the known adverse consequences of disposing with the pyloric control on gastric emptying.

Methods that use implantable active devices (prosthetic sphincters)

The Summers¹², Giori⁷ and Rosen¹⁶ sphincters

The devices reviewed have potential use as artificial enteric sphincters¹¹. They are not a viable possibility in the opinion of the author for the reasons already outlined.

The AMS 721 in a canine ileostomy model⁷⁰

The first study to assess this device in the gastrointestinal tract was performed by Delaney and his co-workers⁷⁰. They implanted the AMS 721 prosthesis in 15 dogs. The purpose of their study was to:

1. determine the sphincter pressure necessary to restrain the passage of intestinal contents
2. measure intraluminal pressure underlying the cuff of the sphincter
3. measure blood flow changes in tissue under the cuff
4. determine short term intestinal tolerance to various cuff pressures and
5. observe chronic changes with long term sphincter activation.

The sphincter pressure was measured directly from the cuff and the intraluminal pressure was measured using a perfused catheter system. The intraluminal pressure was always lower than cuff pressure by approximately 20-55 cmH₂O and was seldom measured to be greater than 40 cmH₂O. Intraluminal pressure correlated with intestinal content holdback pressure. The blood flow was measured by the rubidium dilution method at post mortem and showed that mucosal flow decreased to 50% of baseline at a cuff pressure of 120 cmH₂O. Other intestinal layers were not significantly affected at that pressure. A cuff pressure of 275 cmH₂O for 18 hours uniformly caused necrosis and ulceration. Long -term (three month) observation revealed two main problems: infection and the development of a fibrous

ring around the cuff causing obstruction. Mechanical complications were not reported.

The AMS 721 in a minipig colostomy model⁷¹

Von Schöning and co-workers reported a less successful study in five minipigs with end sigmoid colostomies around which the cuff was implanted in a second stage procedure⁷¹. Test animals developed a range of complications (pump bulb migration and erosion, infections - local and generalized). The sphincters operated in a satisfactory manner, but only one animal survived 60 days with a functioning implanted sphincter.

The Haber patent⁷²

The designer of this device claims that it achieves continence by reproducing the anatomy of the rectal valves (even though the contribution of these inconstant features of the colon to faecal continence has not been established). Activation and deactivation would presumably be achieved by using a control mechanism similar to the AMS 800 sphincter. This device has three active pressure exerting elements (Figure 13). There are, therefore, several places of increased pressure application on the bowel without any pressure dissipating “hammock” effect (see Chapter 3). There is no evidence that this device has been tried clinically in an animal model or in humans.

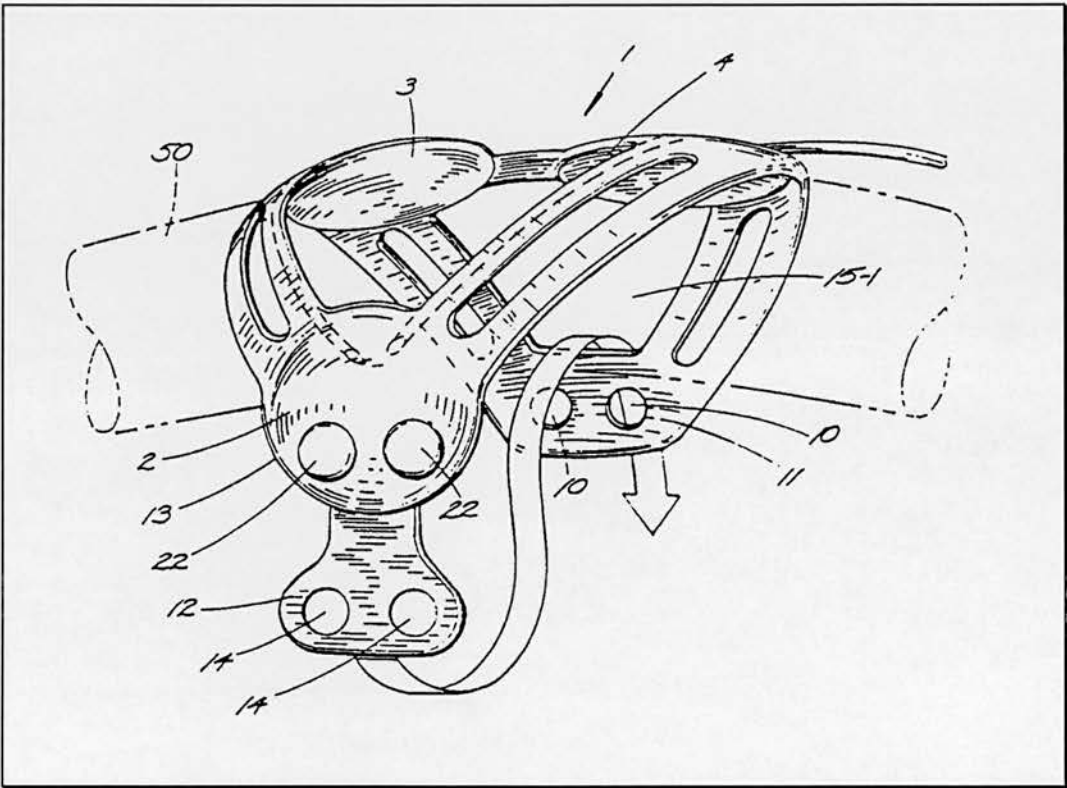


Figure 13: The Haber device⁷² designed to simulate the rectal valves.

The AMS 800 as an anal sphincter^{41,73-75,78-80}

The first report of an AMS 800 like device implantation is by Chandler and co-workers⁸¹. They implanted the artificial sphincter around an ileostomy in 18 female beagle dogs for up to 36 weeks. The control pump used in this study had not been described previously in any of the patent disclosures and there is no evidence that it has ever been used in any other study. It involves a manually activated equilibration channel instead of the typical resistor. This component resulted in unreliable operation of the device. Eight hours of daily occlusion at 50-55 mmHg (68-75 cmH₂O) resulted in dependable continence without causing damage to the bowel. Mucosal thickness was reduced and stunting of villi was observed under the sphincter. Occlusion also resulted in increased accommodatory capacity of the ileum without incurring defects in ileal absorptive or secretory function, but promoted anaerobic bacterial growth. Pressure beneath the cuff (intraluminal pressure) always slightly exceeded holdback pressure, but the slope of both lines was 0.57. This means that the system was set in such a way that approximately 60% of the cuff pressure was transmitted on to the tissues.

Twelve animals died or had to be killed before the study was completed. One half of these were due to small intestinal obstruction or volvulus mostly due to adhesions to the cuff. Two dogs developed obstruction due to the development of a fibrotic ring just proximal to the sphincter cuff. The above complications occurred sporadically as late as 29 weeks after implantation. Two device malfunctions occurred which were due to a faulty one way valve in a pump and a ruptured balloon.

Sofia et al⁷⁸ implanted a version of the AMS 800 with a larger cuff around the rectum/colon in fifteen dogs for up to twelve months. Eight animals had an abdominoperineal resection of the rectum and the rest had their anal sphincter divided in three places. The device was activated two weeks after implantation and they received weekly enemas as they suffered frequent faecal impaction. Continence was maintained in seven out of the fifteen animals for periods of 4-8 hours at a cuff pressure of 50-70 cmH₂O. Period of continence was dependent on cuff pressure (Table 3).

Cuff pressure (cmH ₂ O)	Duration of continence (hours)	Cuff pressure (cmH ₂ O)	Duration of continence (hours)
73	8	29	4
60	8	29	4
50	8	25	4

Table 3: Duration of continence depends on cuff pressure⁷⁸.

Histology revealed mucosal stunting and a degree of fibrosis in all other layers, but no ulceration in these seven animals. Complications observed in the same four out of the fifteen animals were infection, device extrusion/ulceration. Infection was successfully treated in three out of the four cases and the device was successfully replaced in two out of the four instances of extrusion.

Another study was performed in pigs by Satava and co-workers⁷⁹. Thirteen swine were implanted with the AMS 800 prosthesis in two stages: a perineal colostomy was first performed and this included placement of the cuff and intraperitoneal balloon. The control pump was implanted subsequently. The device was activated for 22 hours a day and follow-up duration was two to six months. The clinical and mechanical complication rate was unacceptable (Table 4).

There is little doubt that a combination of factors contributed to the unacceptably high complication rate and death. The pump prototype and other system components were unreliable. The pressure applied by the cuff to the tissues was not measured. The bowel was occluded for a prolonged period by the sphincter.

Number	Continence	Time	Complication	Cause
5 (72%)	Complete			
1	Partial			
1	Incontinent			
3		<5 weeks	Death	Unrelated
3		Prior to activation	Sphincter erosion	? Ischæmia, ?technical
2		2, 4.5 months	Sphincter erosion	? Ischæmia
2			Balloon erosion into bowel	
5 (55%)			Pump skin erosion	Infection, ischæmia
3 (33%)			Pump malfunction	
7 (100%)			Mucosal ulceration	Ischæmia
3	Late incontinence		Cuff securing tab fracture	
9 (69 %)			Death	Various

Table 4: Summary of the results of implantation of the modified AMS 800 sphincter in pigs⁷⁹.

Shoshany and Peña in 1994⁸⁰ implanted the AMS 800 extraperitoneally around the rectum in 12 minipigs using the posterior sagittal approach. Five minipigs had the sphincter activated in a total of 15 occasions. The device was effective in maintaining continence when activated, but the complication rate (infection, erosion, colonic obstruction and mortality) was prohibitive.

In view of these results, it is perhaps surprising that the device was ever implanted in humans^{41,73-75}.

In their study, Heiblum and Cordoba⁸² used an artificial sphincter, again made of silicone elastomer, which was placed subcutaneously around an end

colostomy in six patients. The device used was a simple, wrap-around inflatable cuff, attached to a silicone tube of approximately 5 mm in diameter, through which air was passed to inflate the cuff. Subcutaneous infections developed around the prosthesis in three patients. In two of these, the infection was treated successfully with antibiotics; in one case, the prosthesis had to be removed. In the other five patients, complete continence to stool and gas was achieved.

Christiansen and Lorentzen⁷³ report the first implantation of the AMS 800 device for anal incontinence in a human in 1987. A 67 year old patient with Myasthenia Gravis reportedly benefited from the device: resting anal pressure and squeeze pressure increased as shown in Table 5 after three months. The patient felt that the anal canal was slightly narrow, so faecal softening-bulk forming laxatives were administered. Another complaint was that the sphincter had to be de-activated twice during defaecation as a five minute automatic re-occlusion time was not adequate.

Resting anal pressure (mmHg)		Maximum squeeze pressure (mmHg)	
Pre-operatively	Three months Cuff open	Pre-operatively	Three months Cuff closed
47	53	73	89

Table 5: Summary of anal manometry in first patient with implantation of the AMS 800 sphincter for anal incontinence. Cuff Pressure 66-74 mmHg. Cuff circumference 11 cm.

A report by the same author on five patients followed shortly⁷⁴ followed by a cumulative report on twelve patients⁷⁵ mainly with neurological causes of incontinence (9) but also trauma or absence of the sphincters (3). The device appeared to effective with solid or semi-solid stool but not with diarrhoea. its

effectiveness was also seemingly enhanced by the maintenance of the anorectal angle. The same complaints regarding the feeling of obstructed defæcation were reported by patients suggesting that the cuff circumference should be increased.

A further two patients with anorectal malformations in whom the AMS 800 sphincter has been implanted have been reported⁴¹. One patient was fully continent after one year, whereas the other suffered occasional leakage of liquid and flatus. These early results were encouraging, but the ischæmic complications that were reported when the device was implanted around bowel in urinary diversion procedures (see discussion above) did not encourage the manufacturers to continue the development of the device for the control of fæcal incontinence.

The AASP 2000 Glasgow Neosphincter⁷⁶

It can be seen from the above discussion that urinary incontinence has been successfully treated using an inflatable circular cuff applied to the outer layer of the urethra^{37,44,45,83}, whereas a modified prosthesis of similar circular design when used around bowel in animals and humans, was less successful and also produced intestinal ischaemia at operating pressures which maintain continence^{36,78,79}. This was probably because the rectum is not “circular” and the application of a circular cuff produced *crenation* of the bowel wall in localized high pressure points within the folds³⁷. These early results did not encourage any further research or development of this device.

We have, therefore, developed an artificial anal sphincter prosthesis⁷⁶ (Figure 14) which attempts to simulate the normal physiology of the anorectum.

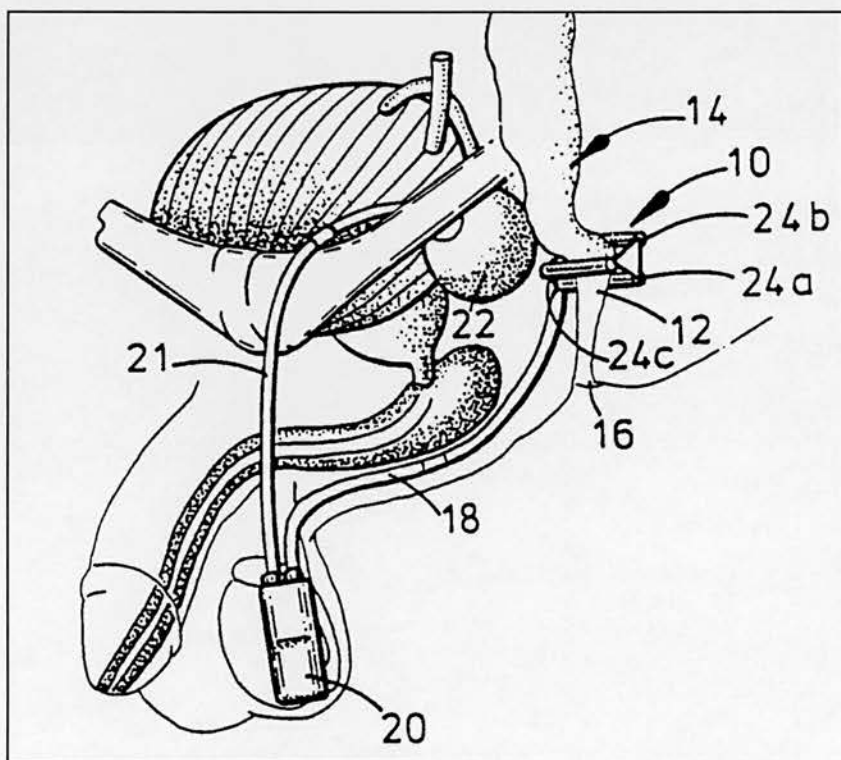


Figure 14: The AASP 2000 Glasgow Neosphincter.

In summary, this device involves a pressure regulating balloon reservoir, a control pump and a sphincter element. The latter consists of a linear inflatable expander (24c) and a silicone gel filled pillow (24a,b) placed transversely across the rectum. Upon activation, the expander gently squeezes the bowel against the pillow. The pressure is distributed evenly by the expander and dissipated smoothly by the hammock effect of the pillow (Chapter 3) thus minimizing the possibility of pressure ischæmia. The device also introduces angulation of the intestine which has been shown to enhance continence and reduce the pressure required to achieve holdback of semi-solid fæces (Chapter 1).

The stages of its design, development and assessment will be detailed in the following sections of this thesis (Chapter 3, Chapter 4, Chapter 6, Chapter 7, Chapter 8, Appendix 3).

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A successful continence device? Review of 4000 complications associated with the AMS Artificial Urinary Sphincter

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Summary

The records of the 4130 complications reported during an eight year period in 3508 patients in whom an artificial urinary sphincter had been implanted were reviewed. 86.6% of patients had only one revision, 10.9% had two revisions, 1.6% and 0.6% had three and four revisions respectively, whereas ten patients (0.3%) had revisional surgery on five to ten occasions. Mechanical complications were reported in 22.1% of cases. 3135 detailed records were further analyzed. In these, 91% of complications occurred in male and 9% in female patients. Complications identified to be related to the mechanical components of the device were reported in 566 patients. These were related to the urethral cuff (48.4%), pump (34.3%), balloon (9.2%), and tubing and connectors (2.6%, 5.5%). Infections were reported in 12.9% of cases. The patterns of total revisions and revisions due to infection followed a double exponential decay curve. 50% of revisions were performed within eight months and 90% within three years of implantation. Complications were still reported up to 17.5 years post implantation. The implications for the design of artificial implants are discussed.

Introduction

A significant contribution to the treatment of urinary incontinence has been the introduction of the inflatable artificial urinary sphincter. Artificial urinary sphincter implantation is currently an accepted form of treatment due to urethral insufficiency¹⁻¹¹. However, acceptance within the urological community was slow because of the complications or mechanical complexity of the previous designs and the initial high rate of postoperative complications^{12,13}. Since the initial AMS 721 model was implanted in June 1972¹⁴, the device has undergone multiple modifications and improvements³ leading to the development of the current model^{15,16}, the AMS 800. This device is now more reliable and both its operation and the insertion procedure have been simplified. The increasing understanding of the effects of the device on the bladder, in combination with more appropriate patient selection and monitoring¹⁷⁻²⁰ has led to a reduction of complications and contributed to the growth of its acceptance and use in recent years. This model is now the gold standard for the patient requiring an artificial urinary sphincter. It is a contractual obligation of the implanting Surgeon/Medical Unit to report any complications and also to return the explanted components to the manufacturer for examination. All complications/revisions are summarized and kept on a database by the FDA which is available in the public domain. This review analyzes the reports between 12/02/86 and 21/06/94.

The results are related to the estimated numbers of implanted devices per year and the complication rates reported previously in smaller studies.

Methods and Design of the Study

This study is a retrospective review of patient reports recording complications while implanted with the AMS artificial urinary sphincter during the period between February 1986 and June 1994 (8.4 years).

Source of information: Diogenes Database which includes the FDA (USA) Pharmaceutical Information and Medical Device Reports (MDR) complication list. The results of the search were obtained on microfilm²¹. The raw data were manually extracted from the microfilm and summarized for each patient by the author. A 42 field computerized relational database was designed and constructed by the author in order to analyze the data. The main database fields included date and duration of implantation, number of revision, sex, patient diagnosis, infective/mechanical complications for each component of the device (pump, balloon, cuff, connectors and tubing), presence of urethral erosion and tissue migration.

Some of the early records were incomplete and these were not included in the final analysis. The results are analyzed according to the following categories:

- General aspects, duration of implant, sex, diagnosis.
- Infection.
- Urethral erosion and tissue migration.
- Iatrogenic complications
- Mechanical malfunction and complications caused by each of the components.

The results were plotted with a curve fitting computer program by a least squares iterative process using the Marquardt-Levenberg Algorithm. The lines were drawn using a cubic spline interpolation method.

The world literature on artificial urinary sphincters was reviewed and marketing data on the AMS devices were obtained from the manufacturers' publications. The reported results are related to the above analysis.

Results

General

The reports reviewed produced 4130 entries for 3508 patients. These included multiple revision procedures in the same patients. 86.6% of patients had only one revision, 10.9% had two revisions, 1.6% and 0.6% had three and four revisions respectively, whereas ten patients (0.3%) had revisional surgery on five to ten occasions (Figure 1). 3690 reports involved the AMS 800 sphincter and 71 involved previous AMS models which were replaced by the AMS 800 either routinely or after malfunction.

3135 detailed records were further analyzed. In these, 91% of complications occurred in male and 9% in female patients. The original diagnoses of the patients with the implanted sphincter (male and female) are summarized in Figure 2.

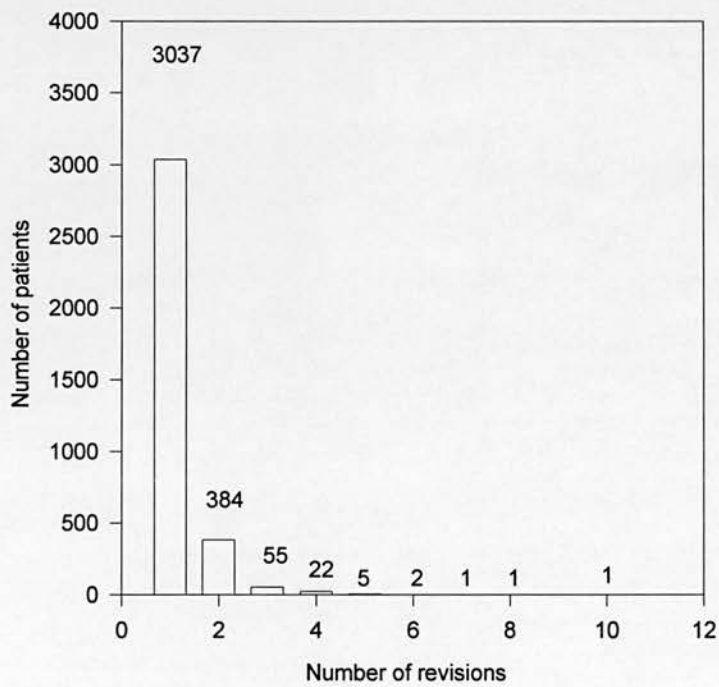


Figure 1: Number of revisions (n=4130) in 3508 patients. Most patients (86.6%) had only one complication requiring intervention.

The complications are broken down according to the initial diagnosis and these are summarized in Chart 1 (male patients) and Chart 2 (female patients).

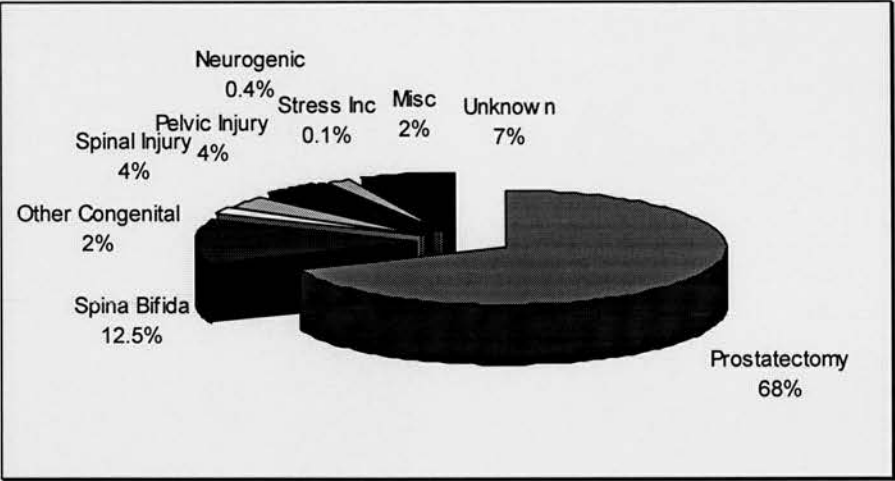


Chart 1: Initial diagnosis of male patients with complications.

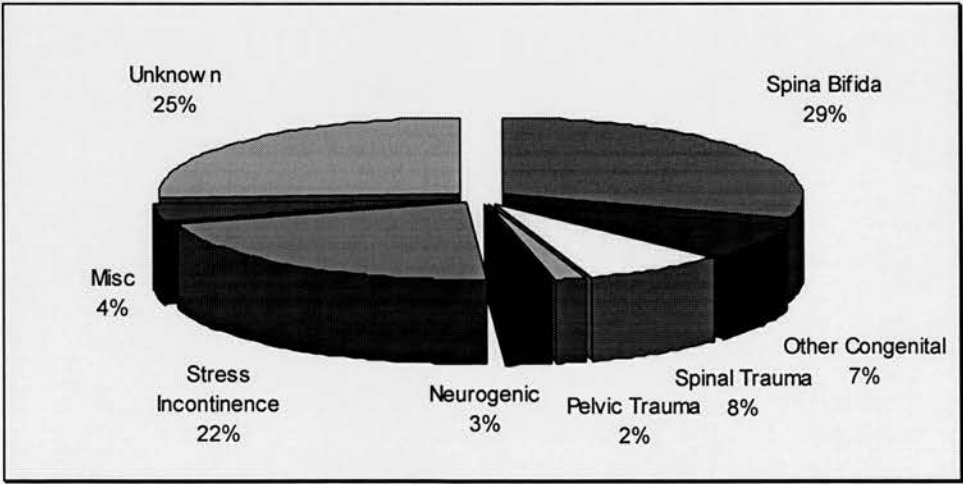


Chart 2: Initial diagnosis of female patients with complications.

The miscellaneous diagnosis group consisted of a small number of each of the following conditions: abdominal aortic aneurysm repair and pelvic neuropathy,

bladder neck incision, cerebral palsy, cystic fibrosis, cystitis, dementia, diabetic neuropathy, epispadias, exstrophy, multiple sclerosis, myasthenia gravis, myelodysplasia, peripheral vascular disease, rectourethral fistula, sacral agenesis, sacrococcygeal teratoma, urinary undiversion.

Most revisions took place during the first year post implantation. The number of revisions declined with time (Figure 3 and Figure 4) and followed a double exponential decay relationship (Table 1). 50% of revisions were performed within eight months and 90% within three years of implantation. Complications were still reported up to 17.5 years post implantation.

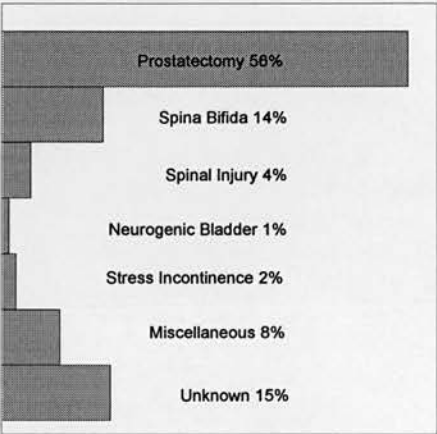


Figure 2: Artificial urethral sphincter implants by aetiology in 3135 patients with complications.

Figure 3 shows a histogram of the number of complications reported per year post implantation. The longest interval between implantation and revision reported was 17.5 years. This was the first complication reported in a male patient who suddenly became incontinent. This was found to be due to pump failure of a previous model of the sphincter (probably AMS 742) which had been implanted in January 1976. The device was changed to the new model in May 1993.

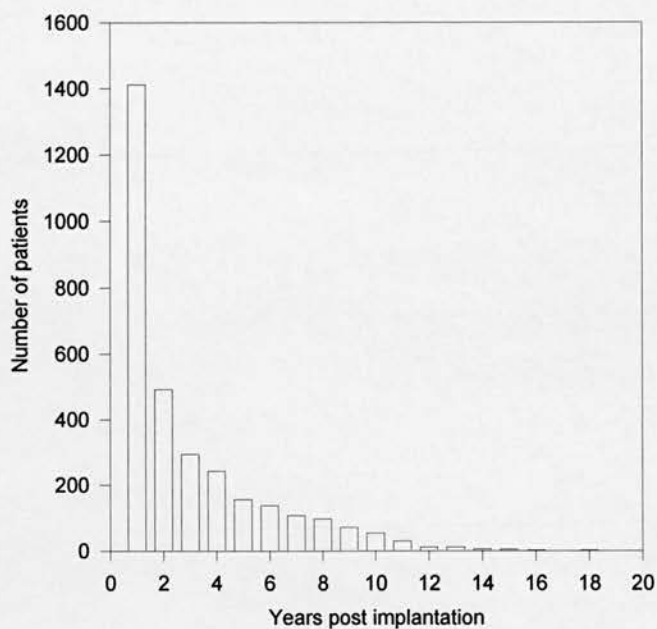


Figure 3: Histogram of the number of revisions performed each year in the 3508 patients.

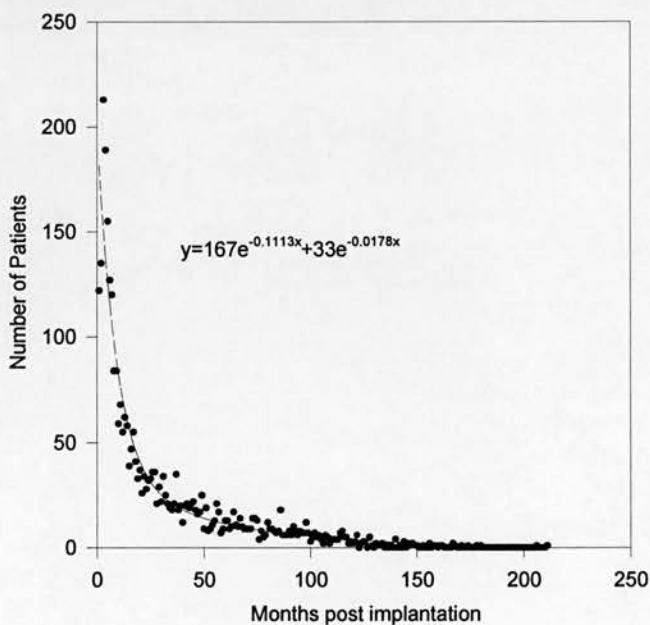


Figure 4: Number of revisions performed each month after implantation in the 3508 patients. The line represents a double exponential decay equation fitted to the data.

	N	Equation	Dependence coefficients
Revisions (total)	3135	$y=167e^{-0.1130x}+33e^{-0.0178x}$	0.74, 0.88, 0.96, 0.87
Infections (total)	404	$y=360e^{-0.1391x}+4.5e^{-0.0263x}$	0.81, 0.90, 0.97, 0.89
Pump infections	284	$y=27e^{-0.1483x}+3.2e^{-0.0263x}$	0.81, 0.91, 0.92, 0.89
Balloon infections	275	$y=27e^{-0.1476x}+2.7e^{-0.0248x}$	0.79, 0.90, 0.97, 0.89
Cuff infections	299	$y=29e^{-0.1690x}+3.6e^{-0.0256x}$	0.72, 0.88, 0.95, 0.80
Urethral erosion	432	$y=29e^{-0.1552x}+8.2e^{-0.0312x}$	0.85, 0.92, 0.98, 0.91
Tissue migration	127	$y=8.2e^{-0.1370x}+0.3e^{-0.00086x}$	0.57, 0.78, 0.92, 0.89
Pump (mechanical)	95	$y=24e^{-0.2162x}+1.4e^{-0.0133x}$	0.61, 0.77, 0.83, 0.73
Balloon replaced to increase pressure	271	$y=20e^{-0.0481x}+12e^{-0.0516x}$	1.00, 0.99, 1.00, 0.99

Table 1: Parameters of exponential equations governing the revision data.

Infection

There were 472 reports of infection of the device or its components out of the 4130 complications (11.4%). Out of these, 404 had complete records and were further analyzed: the infection rate was 12.9%. In 224 of these cases (55%) all three components were reported to be infected. The breakdown of the infections is summarized in Table 2 for complete and incomplete records.

The timing of infections is shown diagrammatically in Figure 5 - Figure 9 and the equations describing the exponential decay with time appear in Table 1.

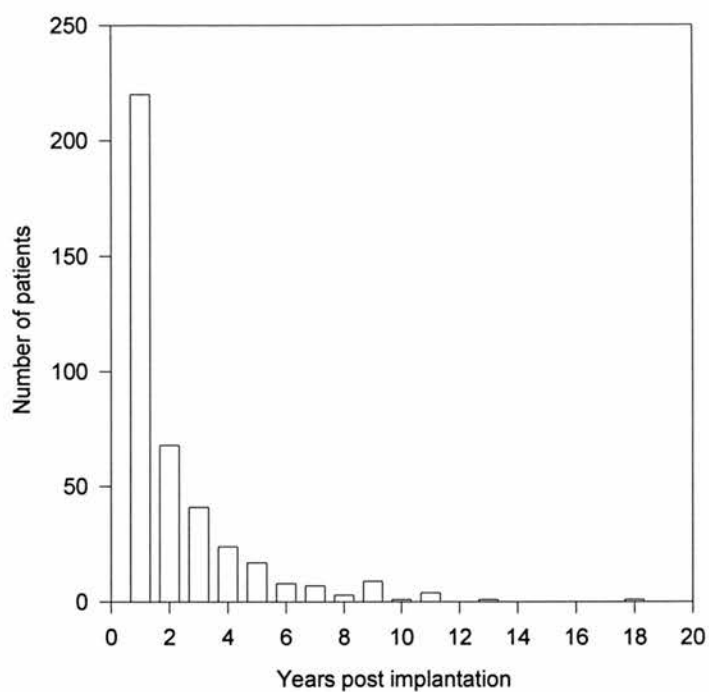


Figure 5: Histogram of the timing of infection of the device post implantation. 404 patients with complete records.

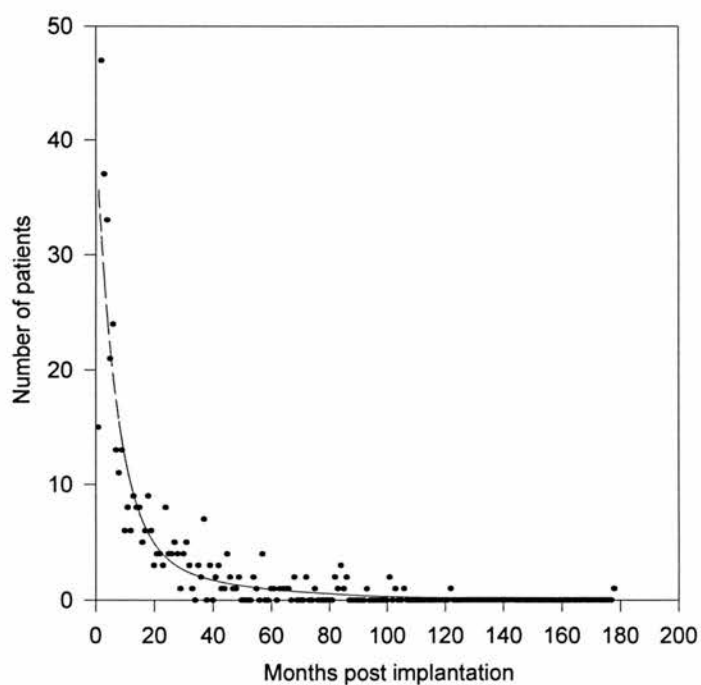


Figure 6: Breakdown of developing infections suffered by the 404 patients.

Infection	n=4130, (%)	% of total infections	n=3135, (%)	% of total infections
Any infection	472, (11.4%)	100%	404, (12.9%)	100%
Pump infection	316, (7.6%)	67%	284, (9%)	70%
Balloon infection	302, (7.3%)	64%	275, (8.8%)	68%
Cuff infection	321, (7.8%)	68%	292, (9.3%)	72%
All components	244, (5.9%)	52%	224, (7.1%)	55%

Table 2: Breakdown of infective complications in all case reports (n=4130) and also in cases in whom duration of implantation is known (n=3135).

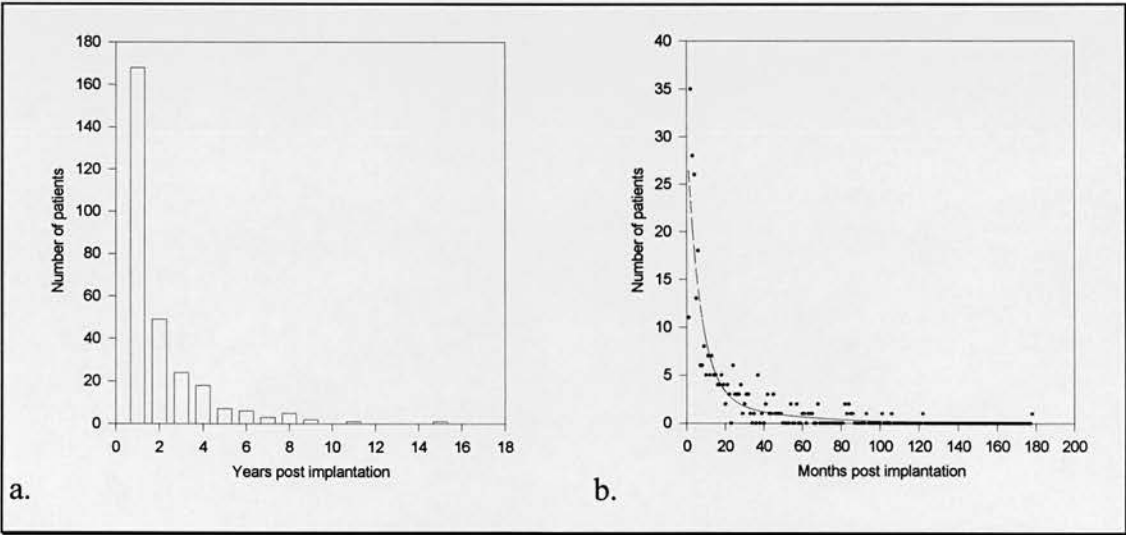


Figure 7: Timing of pump revision due to infection in 284 patients. a. Yearly breakdown, b. Monthly breakdown.

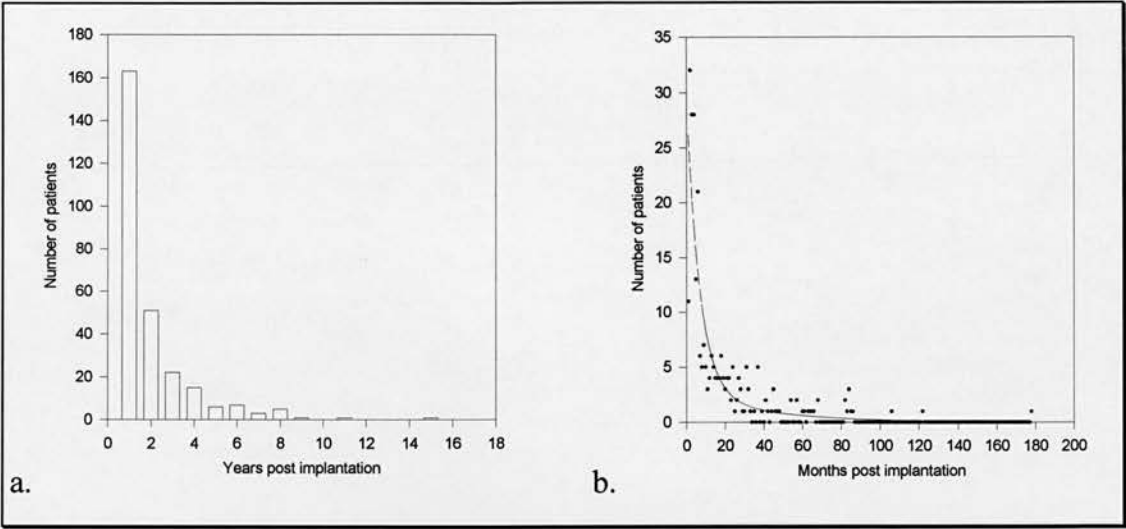


Figure 8: Timing of balloon revision due to infection in 275 patients.
a. Yearly breakdown, b. Monthly breakdown.

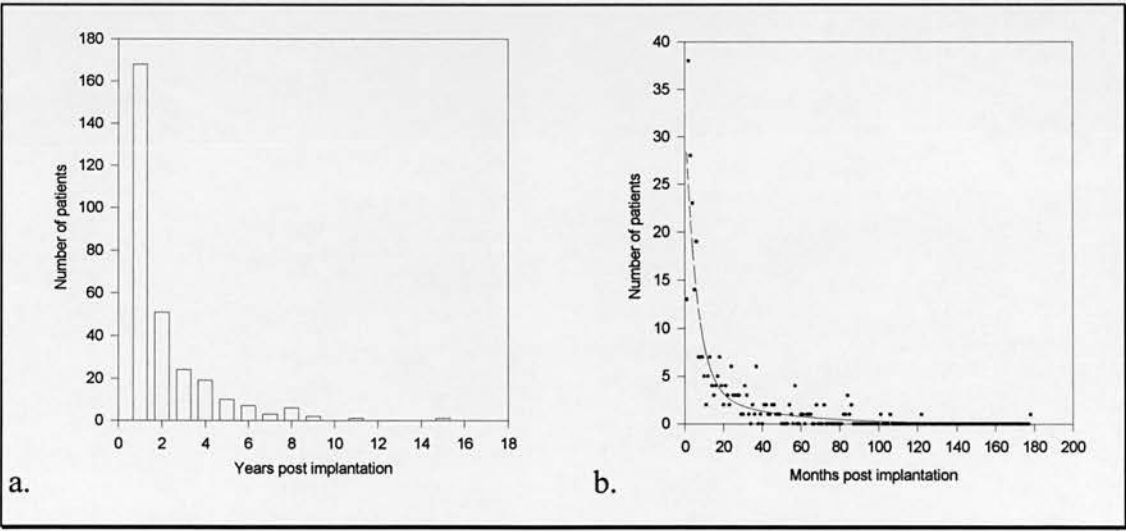


Figure 9: Timing of cuff revision due to infection in 292 patients.
a. Yearly breakdown, b. Monthly breakdown.

Urethral erosion and tissue migration

There were 432 reports of patients suffering urethral erosion. The timing of this complication also follows a double exponential decay relationship (Figure 10,

Table 1). This complication was reported as late as 14 years post implantation. In 18 of these patients the urethral erosion was reportedly associated with the presence of cuff infection (Figure 11). All of the erosions in the presence of infection occurred within six years of implantation. There were also five reports of urethral erosion related to the passage of a urethral catheter; these developed between 10 and 18 months after implantation.

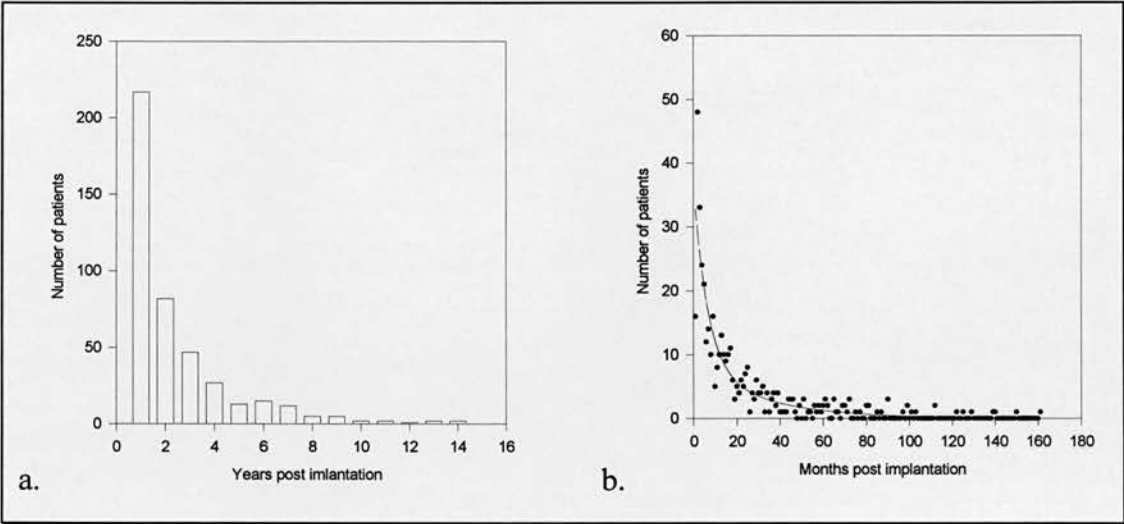


Figure 10: Timing of urethral erosion in 432 patients.
a. Yearly breakdown, b. Monthly breakdown.

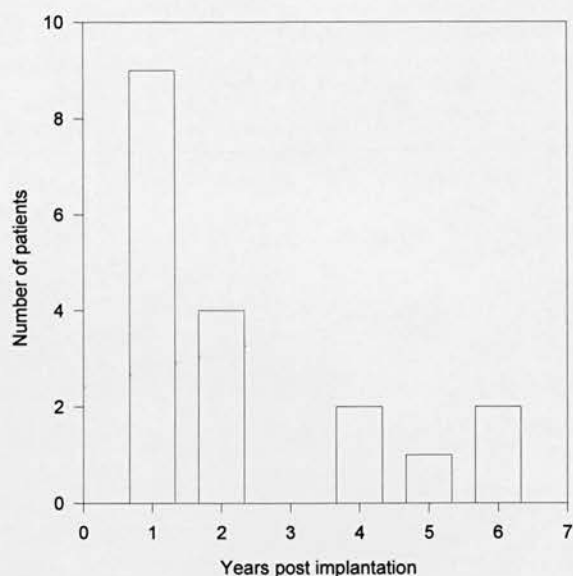


Figure 11: Timing of urethral erosion and simultaneous infection in 18 patients

There were 127 reports (3.1% of complications) of the device components (excluding the cuff) migrating into other tissues, the greatest proportion (59.8%) being caused by the pump (Table 3). In 83 of these the tissue of migration was reported: abdominal wall (15=18.7%), bladder (9=10.7%), colon and rectum (4=4.5%), labia (7=8.4%), retroperitoneum (1=1.2%), scrotum (33=39.7%), testis (2=2.4%), vagina (11=13.2%), wound incision (1=1.2%).

Component eroding	Number	(%)
Pump	76	59.8%
Balloon	22	17.3%
Tubing	11	8.7%
Unknown	18	14.2%

Table 3: Breakdown of tissue migration of the sphincter components (excluding the cuff) in 127 cases.

The timing of tissue migration of components (excluding the cuff), is shown in Figure 12. There appears to be a delayed rise in the incidence of this complication (Figure 12a) which is reported to occur even after 10 years post implantation. An exponential decay relationship can once again be plotted (Figure 12b), but the mathematical fit is less precise for this (Table 1). The dotted line of the plot in Figure 12b represents a sixth order polynomial regression of the monthly data ($r^2=0.72$) which demonstrates this late rise.

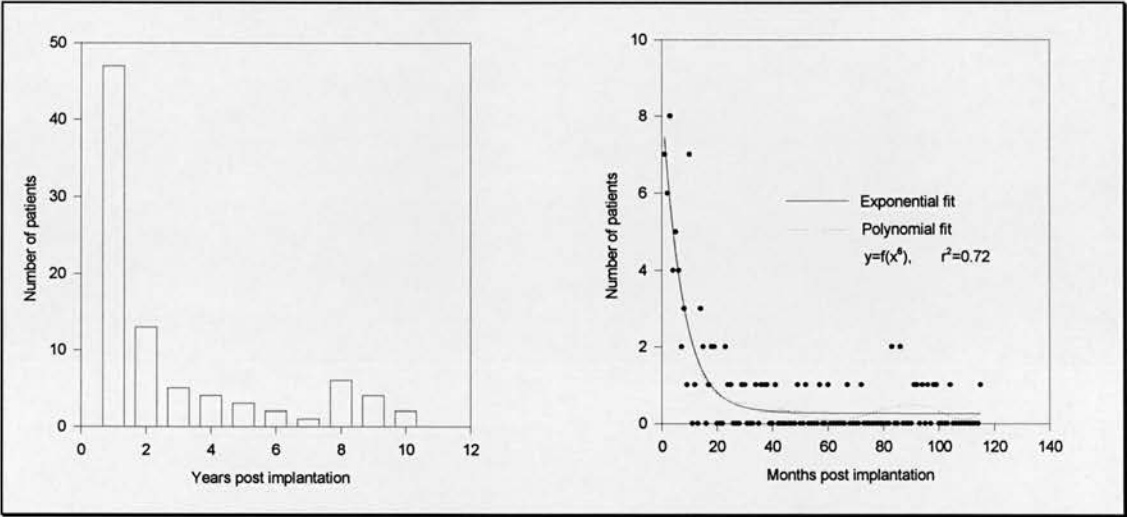


Figure 12: Timing of urethral erosion in 127 cases.
a. Yearly breakdown, b. Monthly breakdown.
Exponential and polynomial regression curve fit of the data.

Iatrogenic complications

There were 26 reports of iatrogenic complications (0.6%). In 22 cases (85%) the urethra was injured. There were two reports of bladder and one report of rectal injury. In the remaining case, the cuff was inadvertently placed around the vagina.

Mechanical malfunction and complications caused by each of the components

These accounted for 22.1% of the total number of complications reported. The total number of cases (4130) and the number with detailed records (3135) are analyzed as shown in Table 4.

	Total (N=4130)		Detailed records (N=3135)	
	n	%	n	%
Pump	325	35.6%	194	34.3%
Balloon	115	12.6%	52	9.2%
Cuff	400	43.8%	274	48.4%
Tubing	27	2.9%	15	2.6%
Connector	47	5.1%	31	5.5%
Total	914	100%	566	100%

Table 4: Breakdown of mechanical complications of the components of the artificial urethral sphincter.

As the distribution between the two types of records is almost identical, the complete records will only be analyzed when temporal data is required (pump, balloon and cuff).

Pump

Failure of the pump was reported in 325 (7.9%) of the patients, accounting for 35.6% of mechanical complications. The reason for the mechanical failure was stated in 95 of these reports (Table 5). Duration of implantation was available in 194 of the 325 patients and this is plotted in Figure 13. The parameters of the exponential decay equation governing this data are shown in Table 1. The longest interval between implantation and revision reported was 17.5 years. This was the

first complication reported in a male patient who suddenly became incontinent. This was found to be due to pump failure of a previous model of the sphincter which had been implanted in January 1976 and this was changed to the new model in May 1993.

Complication	n	Complication	n
Shutoff valve leak	4	Fracture of pump	4
Shutoff valve block	13	Fracture of tube insert	3
Resistor blocked	23	Airlock	22
Resistor flow too fast	11	Fibrosis - stiff pumping	3
Resistor flow too slow	4	Pinhole ?iatrogenic	3
Balloon valve leak	1	Sabotage	2
Cuff valve blocked	1	Twisted tubing	1

Table 5: Description of 95 mechanical complications attributed to the pump.

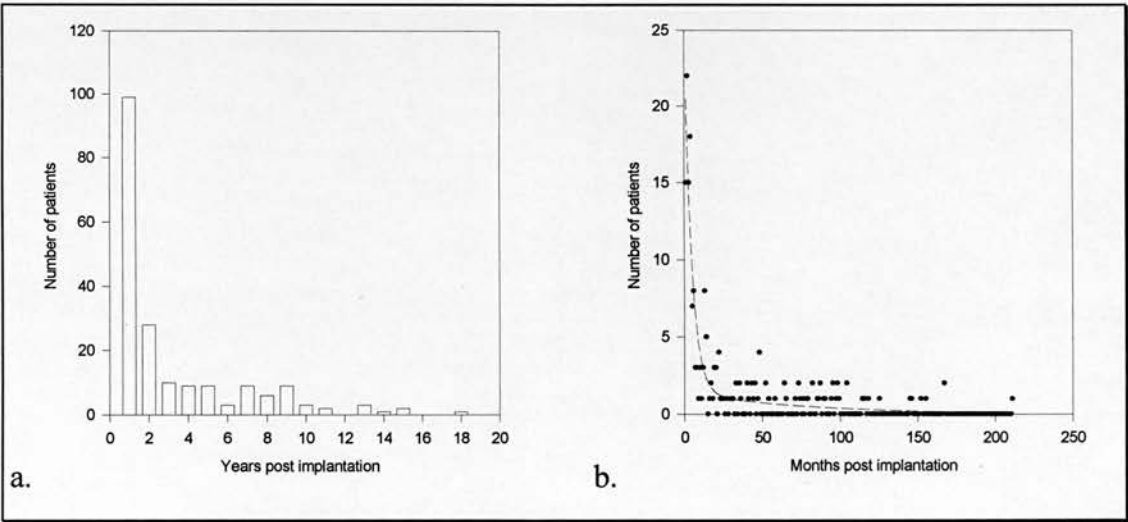


Figure 13: Timing of mechanical complications of pump in 194 cases.
a. Yearly breakdown, b. Monthly breakdown.

Balloon

There were 115 complications over a period of 8.5 years post implantation directly attributable to the balloon. These accounted for 12.6% of the total mechanical complications. Severe atrophy due to a high balloon pressure was reported in 23 (20%) of these cases, tissue migration or displacement was reported in 25 (22%) and rupture or leakage of the balloon in 67 (58%) of cases. There were, however 356 reports of replacement of the balloon to one of a higher plateau pressure due to late onset of incontinence. Duration of implantation data was available in 271 of these and this is plotted in Figure 14.

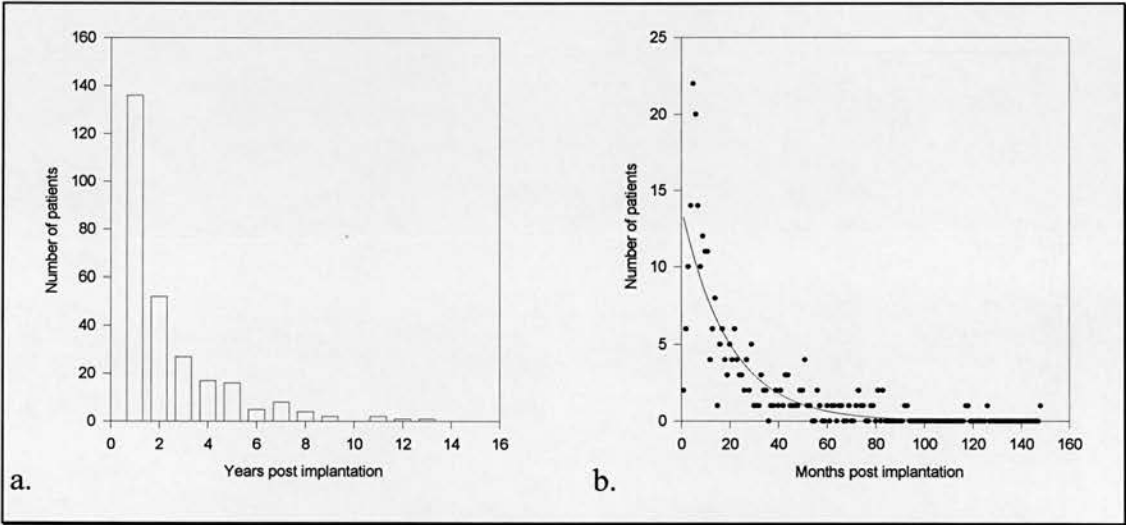


Figure 14: Timing of re-insertion of a higher pressure balloon in 271 cases.
a. Yearly breakdown, b. Monthly breakdown.

Cuff

In 400 cases the cuff was reported to be malfunctioning, making it responsible for 43.8% of mechanical complications. In 155 (39%) of these cases the cuff leaked or ruptured. Duration of implantation details were available in 90 and these are plotted in Figure 15. In five cases (1.25%) there was urethral obstruction

and urinary retention shortly post-op which was probably caused by displacement of the cuff.

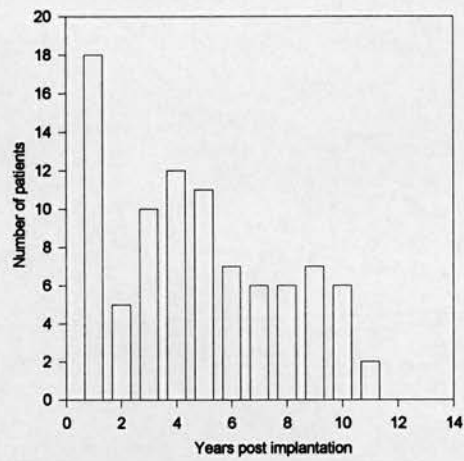


Figure 15: Plot of cuff revisions due to leakage or rupture.

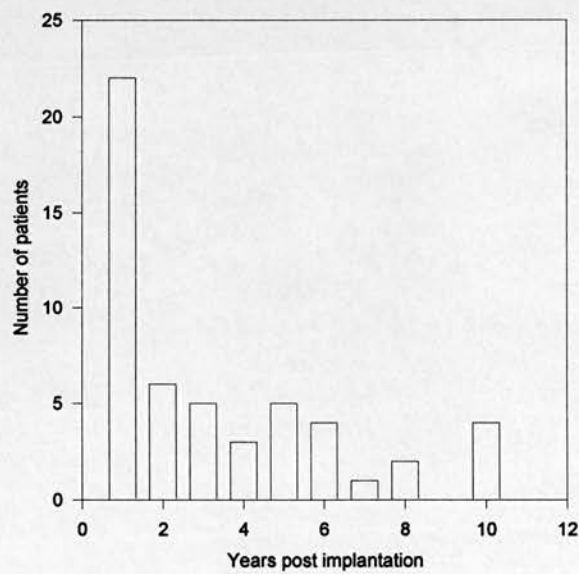


Figure 16: Timing of insertion of additional cuff around the urethra.

A second cuff operated by the same balloon and pump was implanted in 52 patients after the initial report of the procedure in 1993²².

Tubing and connectors

In total 74 complications relating to the above components were reported (1.8% of total records). 27 were related to the tubing and 47 to the connectors. In 8 cases the tubing eroded through the skin. Leaks were attributed to the tubing in 19 cases and to the connectors in 45. There was one incident of a blocked connector and one case where the cuff and balloon were connected the wrong way round. No blockage due to kinking of the tubing was reported. Overall, these components were responsible for 8% of mechanical failures.

Literature Review

A literature review on the artificial urinary sphincter was also performed. This chapter will concentrate on the results of the AMS family of devices (the other reported devices are described in the previous chapter and in Appendix 3). The main findings of the published reports on the AMS sphincter are summarized in Table 6. Out of a total of 3321 patients, 275 (8.3%) were implanted with non AMS 800 models (the breakdown of these was as follows: 7.6% AMS 721, 21.1% AMS 742 and 71.3% AMS 791/2).

In analyzing the data, it became apparent that several groups reported their experience in stages as the implant numbers built up. In so far as can be determined from these papers, the latest and most encompassing paper is included in Table 6 in order to avoid duplication of patient numbers. Thus, the patients reported in several earlier reports^{1-5,7-10,12-14,19,23-32} may be included in the latest publications by Scott⁶, Mundy²⁰ and Salisz and Diokno³³ which report on the global/long term experience of their teams.

Ref.	Model	Study period (years)	Follow up (mean, months)	Total	Improved (continent) %	Revisions %	U.E. %	Inf. %	Mech. Failure %
34	742a,b,c			31			6.5	32.2	16
35	721		25	12					8.3
36	various	1		21	38		24	14	
37	various	4		19	79	32			
38	742	2.5	3 to 30	47	(91)		13	4	
39	742a/b/c	1		39	38 (742a), 50 (742b,c)		24(a) 33 (b,c)		

Ref.	Model	Study period (years)	Follow up (mean, months)	Total	Improved (continent) %	Revisions %	U.E. %	Inf. %	Mech. Failure %
40	721, 792	1		15	90 (male), 20 (female)		13.3		54(791) 18(792)
41	721	2.5		11	18	82	27	9	45
41	742b,c	2.5		15	60		24	13	
42	791, 792	2		27	89				5
43	various		3 to 48	30	93		6.5		
44	791, 792	2.5		22			0		
45	791, 792			43					
46	800			41	92.7 (87.8)	26.8	9.6		12.1
47	various	10		31					
48	various		(36)	29	65 (79)	21	7	7	
49	721, 761, 742, 791, 792, 800	10		33	76	18			
17	various			45					
50	800		12 to 14	10	100 (80)				
51	various			47					
52	800			20	90	15			
53	800	2	6 to 12	15	100 (73)				
54	various	6		95	(75)		10.5	10.5	13
55	792(34), 800(10)		18	44	91 (64)	30		10	
56	various			1					
57	800	12	1 to 32, (14)	109	83.5 (92.7)	26.5	3.7	2.7	17.4
58	800		14	4	(100)				

Ref.	Model	Study period (years)	Follow up (mean, months)	Total	Improved (continent) %	Revisions %	U.E. %	Inf. %	Mech. Failure %
59	791(15), 792(13), 800(56)	6		84					53
60	800			117	90	15			
61	800		8 to 55, (35.8)	65		98			
62	721, 761, 742, 791, 792, 800	14		40	82.5	62,5	2.5		7.5
63	800		(25)	46	85		15		13
64	800			11					
65	800	5	7 to 60, (26.2)	42	85 (76)	9			
66	800		35	45	88	60			20
6	All	16		406					
67	800			2	100				
68	800		5	1					
69	various			16	(75)				
70	800	7		62	84 (29)	35			
71	800	5	8 to 66, (40)	24	83 (71)	50	20		
72	800			4					
73	800 (mainly)		48 to 240	39	(87.2-all, 95.5-800)	56 (other), 26 (800)			27
74	various		24 to 72	20					
75	800	8	12,	106	86.3	58.4	28		15

Ref.	Model	Study period (years)	Follow up (mean, months)	Total	Improved (continent) %	Revisions %	U.E. %	Inf. %	Mech. Failure %
			(45.6)						
76	various	7		340	93.3				7
77	800	7	60	36	84(1 year), 62(5 years)	58.3			
78	800			2	100				
79	792, 800	5		44	90 (90)	36	11	6.8	
80	800			2	100				
81	800	5	(30)	45	80	40			
20	All	18		200	95		10.5	5	7
82	800	3	6 to 31, (12)	27	80	39			
83	800		33	2					
84	various	1		25			0	0	
85	800	4	1 to 36, (20)	37	(94)	11			
86	800			13	87 (87)	25	12.5		
87	800			126		9		7	
88	various		6 to 94, (41.6)	166	75.3	19.3	6.6	1.2	7.8
89	800		3 to 36	7	57				
90	800	8		37	90	38			
33	various	12		57					
91	various	9		71					
92	various		12 to 60, (20.3)	18	88			0	22
93	800			64	90	22		4.8	

Ref.	Model	Study period (years)	Follow up (mean, months)	Total	Improved (continent) %	Revisions %	U.E. %	Inf. %	Mech. Failure %
22	800			15	80				
Total number of reported patients: 3321 (male 73.2%, female 26.8%)									

Table 6: Summary of results and complications of implantation of the artificial urinary sphincter from published studies. (References cited chronologically).

Since different studies involve different numbers of patients and each does not report the same types of complications, in order to determine the overall success rates and the global rate of each complication from these studies, the following formula was used:

$$Rate(\%) = \frac{\sum [n \times r(\%)]}{\sum n}$$

Where *n* is the number of patients in each report and
r is the individual rate of the complication reported in each study.

The results are summarized in Table 7.

	Global rate	Number of patients
Improved	84.8%	2017
Fully continent	78.5%	940
Revisions (total)	33.5%	1441
Urethral erosion	11.7%	1169
Infection	6.1%	1045
Mechanical complications	13.9%	1425

Table 7: Calculated global success rates and complications of implantation of the artificial urinary sphincter from the published studies.

Increased detrusor instability resulted from the implantation of the sphincter^{17,27,51,69,74,79,94-97} and deterioration of the upper tracts was also reported in 7.4% of cases^{4,27,51,55,56,62,64,74,79} (28 out of 382 patients) including one patient who developed renal failure and required hæmodialysis⁷⁹.

Implantation of the AUS after previous radiotherapy was reported in several studies^{60,86,93,98-100} and this is not considered an absolute contraindication of implantation, provided strict adherence to operating technique detail and asepsis is observed.

Iatrogenic complications as high as 10.5% of cases were reported in one study³³.

In one study⁹¹, seven patients implanted with the sphincter became pregnant. Three delivered normally and four by cesarean section without any complications. In another study⁷¹, two became pregnant and reported stress incontinence and increased frequency. Both these sphincters were deactivated throughout the third trimester.

There were two cases of insertion of the sphincter in patients with renal transplant⁶⁸. In 64 cases, the sphincter and a penile prosthesis were implanted simultaneously^{61,85}. One group of authors⁶¹ report that this combination does not lead to

increased complication rate, even though in their series of 60 patients the rate of revisions averaged at 0.98 per patient.

The balloon was replaced to one with a higher plateau pressure in 7% of cases²⁰.

Discussion

Approximately 150 to 200 AMS 800 units are sold in the UK every year, with proportional usage in Europe and the USA, which corresponds to a worldwide implantation rate in excess of 2000 units per year (figures from AMS representative). During the period of the review, therefore, approximately 16800 devices must have been implanted, giving a global complication rate of 24.6% for all complications. The implantation by aetiology is reported by AMS¹⁰¹ to be as follows: prostatectomy 59%, spina bifida 12%, spinal cord injury 9%, neurogenic bladder 5%, stress incontinence 5% and miscellaneous 10%. The literature also includes anecdotal reports of its usage in patients with renal transplantation⁶⁸, pregnancy^{71,91} and overoptimistic reports⁶¹ of implantation in conjunction with penile implants^{61,85}. The available figures on implantation by aetiology are almost identical to those reported in this review (Figure 2).

Most revisions took place during the first year post implantation as previously reported⁷⁶. The number of revisions declined with time (Figure 3 and Figure 4) and closely followed a double exponential decay relationship (Table 1). 50% of revisions were performed within eight months and 90% within three years of implantation. Complications were still reported up to 17.5 years post implantation, emphasizing the need for prolonged surveillance of these patients.

Less non-AMS 800 model revisions were reported in the FDA database than in the literature. This may reflect the fact that the database included reports from 1986 onwards, whereas most revisions involving the previous models^{2,3,7,8,13,29,35,38-45,47,55,59,102,103} took place prior to or soon after the introduction of the AMS 800 in 1983.

Infection rate of 11.4% to 12.9% is suggested by the analysis in this review, which is higher than the overall reported in the literature (6.1%). Assuming that the 4130 reports in the FDA database come from a population of approximately 17000 implanted patients, then the complication rates should be divided by a factor of ≈ 4 to account for that, and thus to reflect the global patient complication rate (this assumes

that the annual marketing data obtained verbally are accurate and remained constant throughout the period of the review). The infection rate of all three components of the prosthesis becoming infected together represents approximately 6-7% of the complications in this analysis. As a rule, both early (possible contamination during the implantation procedure) and late infections were reported to the FDA, whereas only documented infection of the whole prosthesis was consistently reported in the literature. This may be reflected in the mathematical analysis of the decay curves (Table 1, Figure 9): the exponential time decay coefficients are almost identical for the total number of infections and infection of each component separately, whereas the amplitudes are almost equal only for the individual components (Table 1). This indicates a residual number of infected cases at the start of the analysis, which may represent the numbers of early contamination during the procedure.

The urethral erosion rate in this review is approximately 13.8%. The calculated global rate reported worldwide is 11.7%. The timing of this complication also follows a double exponential decay relationship (Figure 10, Table 1). The balloon pressure in the cases with urethral erosion was not reported consistently in the reviewed papers, making analysis impossible. In one study³⁸, all patients with urethral erosion had been implanted with balloons with plateau pressures >80 cmH₂O. None of the patients who had reservoirs with pre-selected pressure <70 cmH₂O had urethral or vesical neck erosion.

This complication was reported as late as 14 years post implantation and all of the erosions in the presence of infection occurred within six years of implantation. This again emphasizes the requirement for long term follow-up. There were also five reports of urethral erosion related to the passage of a urethral catheter; these developed between 10 and 18 months after implantation. Self catheterization has been reported as an adjunct to artificial sphincter implantation in cases of incomplete bladder emptying⁴⁴. The low rate of this complication in this review indicates that careful self catheterization may be safe.

Much of our knowledge on pressure tolerance of tissue beneath the AMS 800 sphincter come from the experiments of Engelmann and his group¹⁰⁴⁻¹⁰⁶. This was implanted around intestinal loops in 22¹⁰⁴ and 40¹⁰⁵ New Zealand rabbits to evaluate its possible use for continent urinary diversion. This evaluation included the effects of varying closing pressures of the cuff on these isolated bowel loops. Six-weeks postoperative investigations included pressure/flow studies, autopsies, microangiography and histologic evaluations. The sphincter was able to achieve continence during perfusion of the intestinal loop, maximum pressures being dependent on cuff pressures. However, sphincter-related complications (infection, erosion and atrophy of bowel beneath the cuff) were pressure dependent and seen mainly in high pressure groups (Table 8).

Cuff Pressure (cmH ₂ O)	Number of animals	Number of erosions (%)
0	6	1 (16.7%)
40	4	1 (25%)
60	5	2 (40%)
80	7	2 (28.5%)
100	4	4 (100%)

Table 8: Pressure tolerance of the rabbit small intestine^{104,105}.

In a canine model (n=24), balloon pressures of 70 to 80 cmH₂O were well tolerated by the bowel for up to 29 weeks with no evidence of erosion¹⁰⁶. The human sigmoid colon tolerates 70 cmH₂O whereas ischaemic erosion occurred at balloon pressures of 81-90 cmH₂O¹⁰⁶. If we assume that the sensitivity of the urethra to ischaemic injury is similar to that of colon, then the 61 to 71 cmH₂O balloon should be implanted at the first procedure. The actual pressure applied on the tissues is even

lower as only part of the cuff pressure can be transmitted. This is of the order of 60% to 75%.¹⁰⁵⁻¹⁰⁹ (see also, Chapter 3, Chapter 4, Chapter 6 and Chapter 8 for the setting of the sphincter pressure and tolerance of porcine and human colon to sphincteric compression).

Pressure atrophy occurs to a certain degree in all patients and may be due to tightness of the cuff or a high balloon pressure. At a certain critical point (usually four months post activation), cuff efficiency diminishes since there is inadequate pressure transmitted to the underlying tissues and this presents clinically as recurrence of stress incontinence. Correction requires re-operation to insert a smaller cuff or replace the balloon to one with a higher pressure plateau. Due to the safety feature of the balloon plateau pressure, merely injecting fluid to the system does not restore cuff efficiency. Change of the balloon to one with a higher plateau pressure due to subsequent development of stress incontinence was necessary in 8.6% of the patients reported to the FDA. The figure of 7% was reported in one large series²⁰. This cannot be a complication solely attributable to the balloon as there was no evidence of mechanical failure in these cases, nor could it be related to a properly sized cuff being too loose at implantation. The cause was almost certainly a combination of gradual tissue atrophy deep to the cuff in addition to slow leakage of fluid from the system by diffusion. This is corroborated by the delayed onset of this complication.

Another measure which was introduced to decrease the incidence of urethral erosion was primary deactivation³⁸. The device remains deactivated for the period of post-operative healing (typically six weeks) and is activated subsequently. This involved a subsequent surgical procedure to inject fluid in the system or connect the control pump^{38,41,103}. The necessity of this was obviated when the AMS 800 model was introduced¹⁶ which includes a manual long term deactivation button (shutoff valve). This allows the device to remain deactivated and can be activated for the first time by percutaneous manipulation^{58,65,81}. In order to further reduce the incidence of ischaemic complications it has been suggested that the device be kept deactivated during the night as well^{57,58}.

Another way to rectify stress incontinence was reported more recently and involves the implantation of two cuffs in tandem²² claiming success in excess of 95%.

As there was a significant incidence of upper tract deterioration^{4,27,51,55,56,62,64,74,79} and exacerbation of detrusor instability^{17,27,51,69,74,79,94-97} post implantation, it is important that full urodynamic assessment is performed prior to implantation. If the bladder capacity or compliance is low, or if there is detrusor instability, augmentation cystoplasty or a similar procedure should be considered at the same time as artificial sphincter implantation^{17,19,27,28,79,95,110,111}. Long-term follow-up of these patients is, therefore essential.

The device components (excluding the cuff) migrated into other tissues in 3.1% of the patients, the greatest proportion of these (59.8%) being caused by the pump (Table 3). The AMS pump is an extremely light, sub-miniature device. For it to cause relatively so many complications indicates that the design, size and shape of this component is critical (see Chapter 3 and Appendix 3).

There appears to be a delayed rise in the incidence of tissue migration of components (Figure 12) which is reported to occur even after 10 years post implantation. An exponential decay relationship can once again be plotted (Figure 12b), but the mathematical fit is less precise for this complication (Table 1). The dotted line of the plot in Figure 12b represents a sixth order polynomial regression of the monthly data ($r^2=0.72$) which demonstrates this rise which indicates a significant late morbidity.

Implantation of the AUS after radiotherapy was reported in several studies^{60,86,93,98-100}. Mundy considers this a relative contraindication of implantation^{20,99}, quoting an erosion risk of 57%. Despite reports to the contrary^{93,100}, the risk of urethral erosion after implantation in these circumstances appears to be increased^{60,86}: urethral erosion was reported in two of 20 patients (10%) with previous pelvis radiotherapy, compared to 5 of 95 (5.3%) in the non-irradiated group⁶⁰. In another study⁸⁶, urethral erosion in 16 patients (13 who had

undergone external beam radiotherapy and three with Iridium implants) was 12.5%. As the urethral erosion rates reported above were well within the global rates (13.8% in this review, calculated rate from literature 11.7%), it would seem reasonable that these patients are not deprived of this implant if meticulous technique (including primary deactivation) is adhered upon and patient selection is appropriate.

There were 26 reports of iatrogenic complications (0.6%) in this review. The iatrogenic complication rate was reported to be 10.5% in one study of 57 patients³³, almost exclusively due to injury to the pelvic viscera. This report, however, involved very difficult patients in whom an average of 2.8 anti-incontinence procedures were performed prior to artificial sphincter insertion.

Mechanical failure accounted for 22.1% of the complications reviewed (see Table 4) and ranges between 5% and 78% in the literature (average 13.9%).

Approximately 1/3 of the mechanical complications were related to pump malfunction, the majority of these (40%) due to some malfunction of the fluid equilibrating resistor and 18% related to the shutoff valve. The current AMS 800 pump (see Attempts to achieve continence artificially: A Review and Appendix 3) is an extremely reliable, ingenious yet simple piece of equipment. It has undoubtedly contributed greatly to the clinical success of the device.

The cuff was involved in over 40% of mechanical complications, mainly due to leakage (39%). Leakage was almost exclusively present at the site of a cuff fold.

This cuff consists of an outer, firm monofilament knitted polypropylene (Dacron) backing and an inner silicone pliable cuff shell, which is in contact with the tissues. Once the cuff is placed in position and inflated, the lumen assumes a polygonal shape due to the development of (usually three) cuff folds. This has two disadvantages:

1. The cuff causes "crenation" of tissues into the folds¹¹². These folds represent disproportionately high pressure zones (see Chapter 3) and may contribute to pressure ischaemia/necrosis at that point. The fact that no rotational variation of

the intraluminal pressure was observed in an early study¹⁰⁸ is probably a reflection of the relative insensitivity and poor directional discrimination of the fluid perfused pressure measuring equipment employed.

2. It allows for silicone memory and creep phenomena to weaken the cuff at the fold and eventually cause leakage.

Because of the memory effect, once established, these folds persist so they are present both during inflation and deflation. With deflation, these cuff folds come into contact with the outer monofilament knitted polypropylene backing, resulting in friction between the two inner surfaces of the cuff which becomes significant with repeated pumping. This friction promotes the creep phenomenon whereby the silicone molecules tend to migrate away from one another resulting in thinning. This eventually results in a cuff leak that almost invariably occurs at the apex of one of the folds⁸⁷.

In an attempt to improve the cuff, a lubricant surface treatment was introduced by AMS in 1983: the inner surfaces of the cuff shell were coated with a gel of friction reducing fluorosilicone. A new narrow backed cuff design was also introduced in 1987⁸⁷ in order to address the urethral atrophy problem. The incidence of leakage reported decreased from 12.5%⁹ to 1.3%⁸⁷ and revisions for pressure atrophy from 24.6% to 9%. Both these studies were performed by the same group of investigators and involved similar lengths of follow-up.

The introduction of kink proof tubing and special connectors and tooling for intraoperative tubing connection, may explain the relative paucity of complications pertaining to these components (8% of mechanical complications, 1.6% overall).

The device, however, has several disadvantages:

- Currently the cost is in excess of £2500 and this means that it cannot be readily available to many patients. The current patent¹⁶ will expire in approximately seven years and market competition may eventually solve this problem.

- The contour of the cuff moulding template could be changed to produce a cuff which on inflation would uniformly constrict the lumen²⁰ instead of creating a multiple cushion effect.
- There is no compensation for stress incontinence due to increases in intraabdominal pressure (despite claims to the contrary¹¹), as the resistor is interposed in the fluid path between the cuff and the balloon and the non spring loaded ball valve on the cuff side of the pump¹⁶ does not reliably remain open during fluid surges caused by e.g. coughing. The design of Craggs¹³ includes an intraperitoneal balloon to solve this problem, but the pump mechanism is unreliable (refer to previous chapter and Appendix 3). A new valve has been designed by the author¹⁴ to solve this and other problems as discussed in Chapter 3 and Appendix 3.
- There is no way to alter the hydraulic pressure in the system except by re-operating to exchange the pressure regulating balloon for one with a higher pressure plateau. Mundy²⁰ suggests that this is correctable if an access portal with a self-sealing membrane could be incorporated into the device: this could be impaled transcutaneously to measure and adjust the system pressure. The author disagrees with this suggestion as the system operates at the plateau pressure of the balloon. Thus, the pressure cannot be increased beyond the plateau by injecting fluid until the balloon approaches the point of rupture. This represents a safety mechanism whereby the pressure cannot rise to above the said plateau level which might cause ischaemic injury to the tissues. Otherwise, the only way that this adjustment of pressure may be achieved is to either set the system to operate at a pressure level on the rising slope of the balloon sigmoidal pressure-volume curve (this method was employed by the author in the survival animal experiments, see Chapter 6) or to design a balloon with several plateau levels. The latter is a very attractive idea which, however, might be impossible to implement.
- The balloons are available with plateau pressures of 51-60, 61-70 or 71-80 cmH₂O. If the balloon is required to be changed to the next one in the range, the

pressure of the new unit could be anywhere between 1 and 19 cmH₂O higher. This critical parameter, therefore, should be set to a much tighter tolerance²⁰.

In conclusion, the AMS 800 artificial urinary sphincter is a successful and safe device which, when implanted in carefully selected patients, has a high success rate with relatively low rates of complications. Any attempt to develop another prosthetic sphincter for the human genitourinary or gastrointestinal tract should result in a device with at least comparable engineering tolerances and specifications.

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Section 1

***In-vitro* Experiments and Development**

Chapter 1

Does anorectal angle contribute to faecal continence?

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Summary

Studies were performed using an *in-vitro* model to assess the relative importance of sphincter pressure and anorectal angulation in maintaining faecal continence. Water and a semi-solid material were infused separately into porcine intestine compressed by an inflatable cuff until leakage was observed. Angulation of the bowel with respect of the cuff was 180° and then 90°. With water, holdback pressure was independent of angulation. In contrast, when semi-solid material was used, angling the bowel to 90° increased holdback pressure by at least 100%.

Measurements made in solid tubes demonstrated that both a restriction in the tube and an unconstricted 90° bend produced a resistance to flow of the semi-solid material which was dependent on flow rate.

These data suggest that liquids are retained in the rectum by occlusion pressure alone, whereas the retention of semi-solid material is enhanced by angulation.

Introduction

Fæcal incontinence is a common, unresolved socially devastating condition. Continence depends on the coordinated action of the anal sphincters (internal/external) and the pelvic floor musculature¹⁻⁵. The sphincters produce occlusion pressure over the length of the anal canal, while the puborectalis and levator muscles produce occlusion in the upper anal canal. The puborectalis also produces angulation between the anal canal and the rectum. The presence of an acute angle at this site has been considered important in maintaining continence^{6,7}. Indeed, the postanal repair operation for idiopathic fæcal incontinence was designed to correct the obtuse anorectal angle^{2,8} commonly found in that condition^{9,10}. More recently, the rôle of angulation has been questioned and occlusion pressure has been accorded the major determinant of continence^{11,12}. The relative contribution of each mechanism for the maintenance of continence remains uncertain.

A fuller understanding of the mechanisms of continence is important, since it may allow treatment options to be improved. To this end we have studied, *in-vitro*, the flow properties for fluid and a semi-solid material in both rigid tubes and bowel to determine the relative effects of angulation and occlusion on the resistance to flow.

Materials and Methods

Study 1: Flexible Tube (bowel), liquid and semi-solid material

A circular inflatable cuff (75 mm long, 18 mm wide) was placed around a segment of porcine colon 36 mm wide, with a 1.5 mm wall thickness, in a manner similar to a previously reported model for studying fluid holdback^{13,14}. The cuff and bowel were supported in a rigid frame so that the bowel proximal to the cuff could be placed at an angle of 180° or 90° (Figure 1). The cuff was inflated to a predetermined inflation pressure and water at a flow rate of 1 ml/min was infused into the proximal bowel (placed at 180°) using a syringe driver. The intraluminal pressure at which water leaked through the cuffed portion of the bowel was measured by a 2 mm catheter tipped transducer (Gaeltec Ltd., Skye, U.K.). This was repeated for a range of cuff pressures. The proximal bowel was then placed at an angle of 90° to the cuff and the holdback pressures determined as before. Semisolid material in the form of commercially produced pure collagen aqueous suspension (6% collagen, 94% water) was then infused into the bowel under similar conditions using a ratchet driven injector and holdback pressures measured. All measurements were repeated three times.

The rheological characteristics of the material had been evaluated using a controlled stress rheometer and were found to be comparable to those of faeces¹⁵ (Appendix 2).

Colonic pressure under the cuff was measured at each inflation pressure using the “pullthrough” technique.

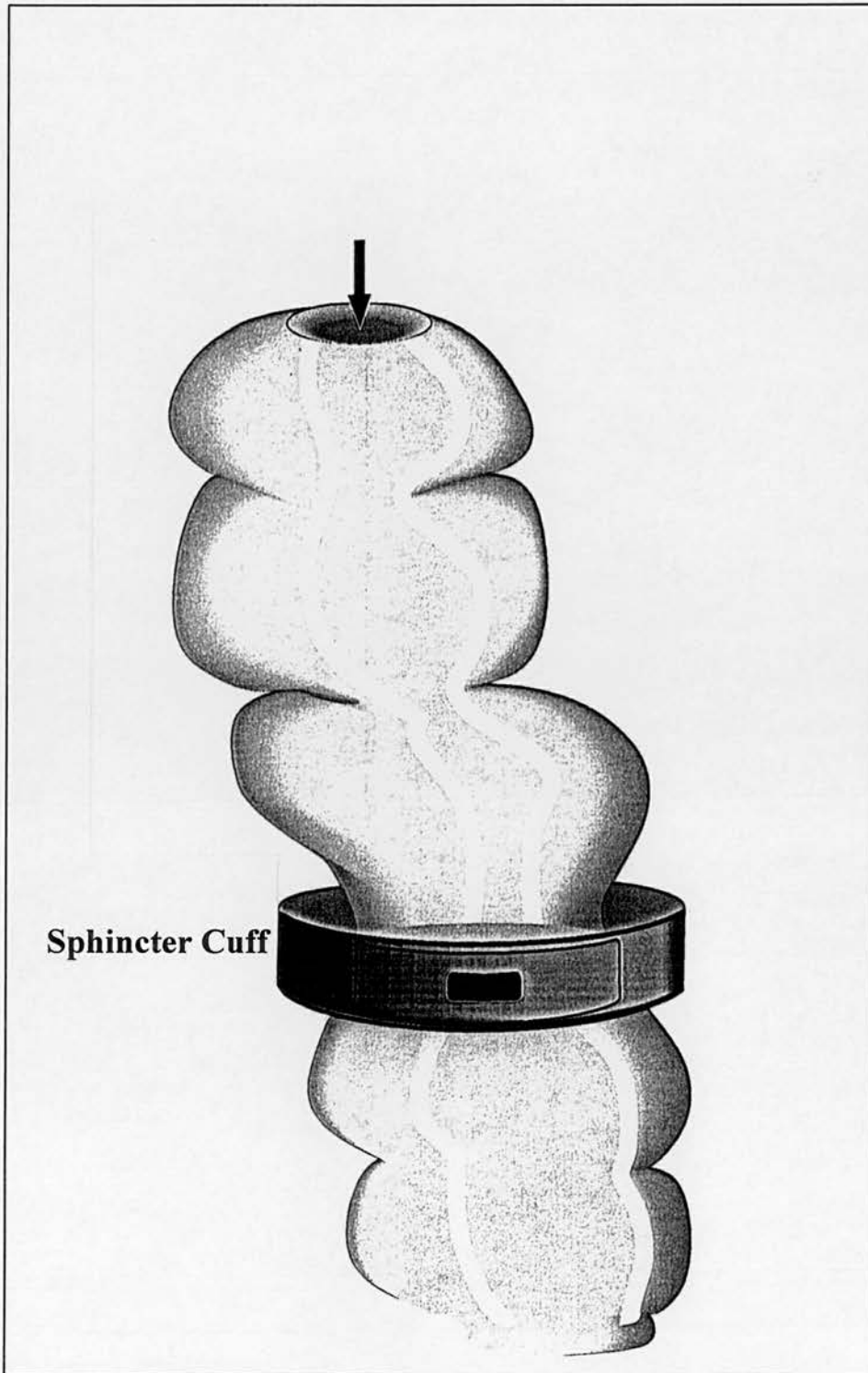


Figure 1: In vitro model for measuring the retention characteristics of bowel at 90° and 180° angulation.

Study 2 : Rigid Tubes, semi-solid material

Three cylindrical glass tubes (diameter 28 mm) were constructed (Figure 2): these were (a) straight, (b) straight with 50% constriction and (c) 90° bend with a constant radius (+/- 2% at apex of angle). A 55 mm long bolus of the collagen suspension was placed in each tube in turn. The inner surfaces of the tubes were first coated with a 1% aqueous solution of hydroxypropyl-methylcellulose which simulated the lubricant properties of colonic mucus and ensured that there was an airtight seal between the bolus and the tube. Air pressure was applied to the end of each tube using a syringe pump. The pressure when the flow of the bolus became constant (see Figure 3) was noted and the experiment repeated at flow rates between 20 and 120 ml/min (linear velocity of approximately 3 to 20 cm/min). These flow rates were chosen to approximate that of faeces during defaecation¹⁶ (64 seconds for complete evacuation). The experiment was repeated with the constricted (Figure 4, Figure 5) and angled tubes (Figure 6, Figure 7).

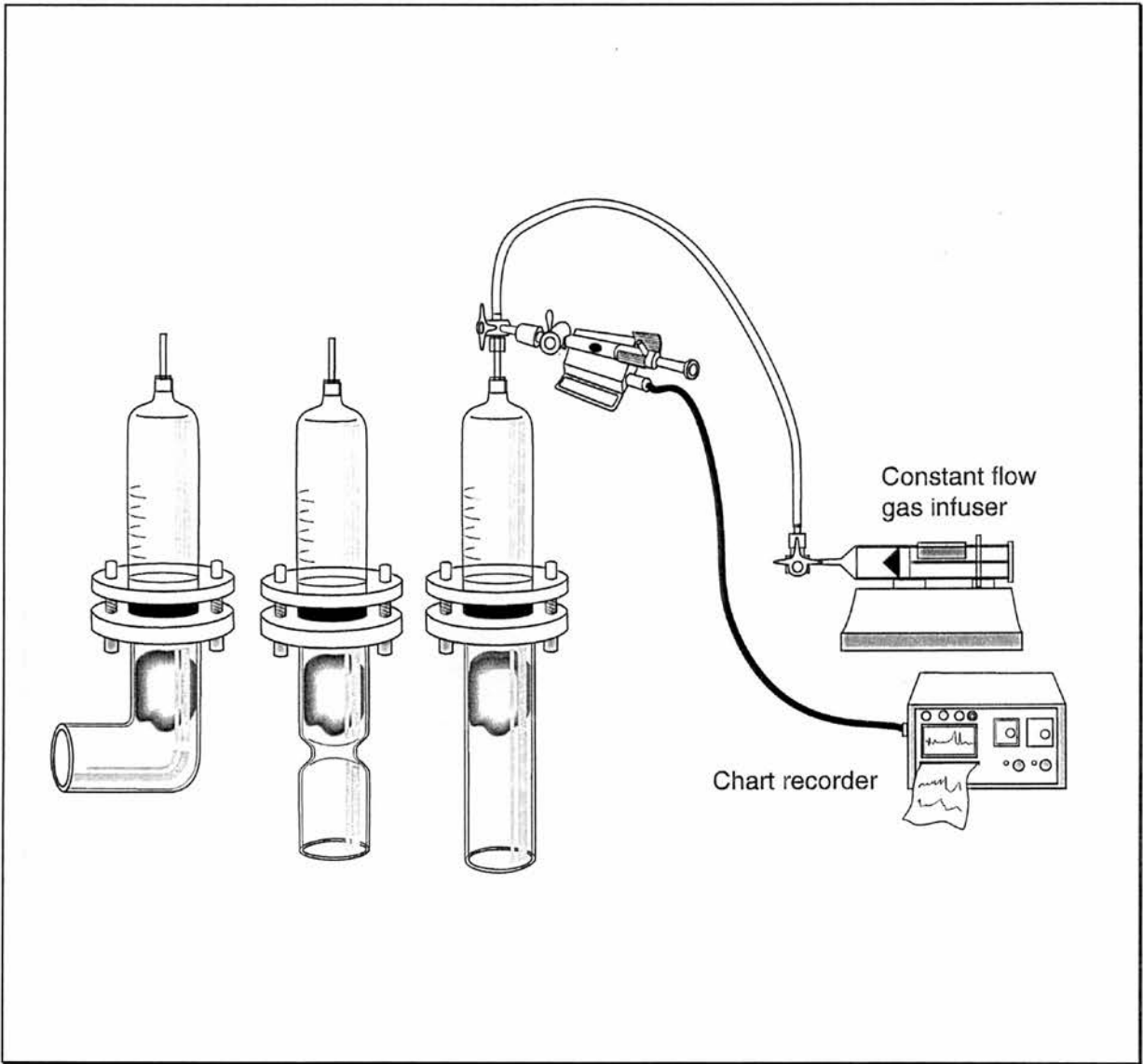


Figure 2: Experimental setup for studying semi-solid material flow in glass tubes.

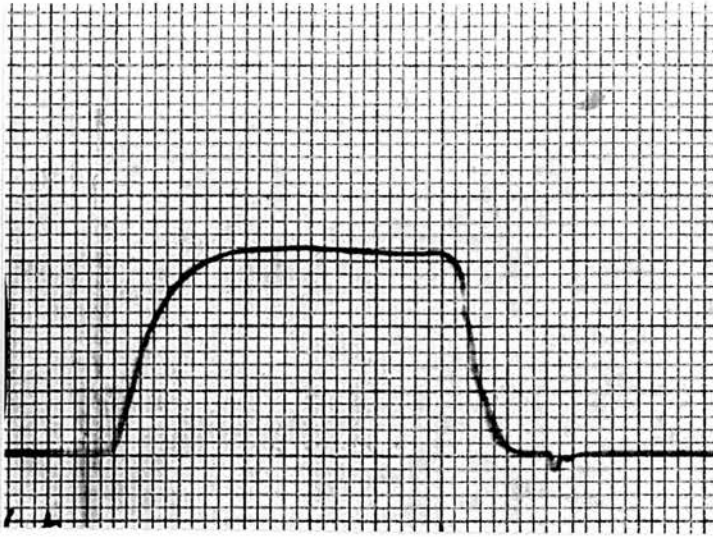


Figure 3: Recording of pressure to achieve flow (y axis) of semi-solid collagen gel in a straight glass tube without a constriction versus time. Pressure reading is taken when flow becomes constant (plateau).

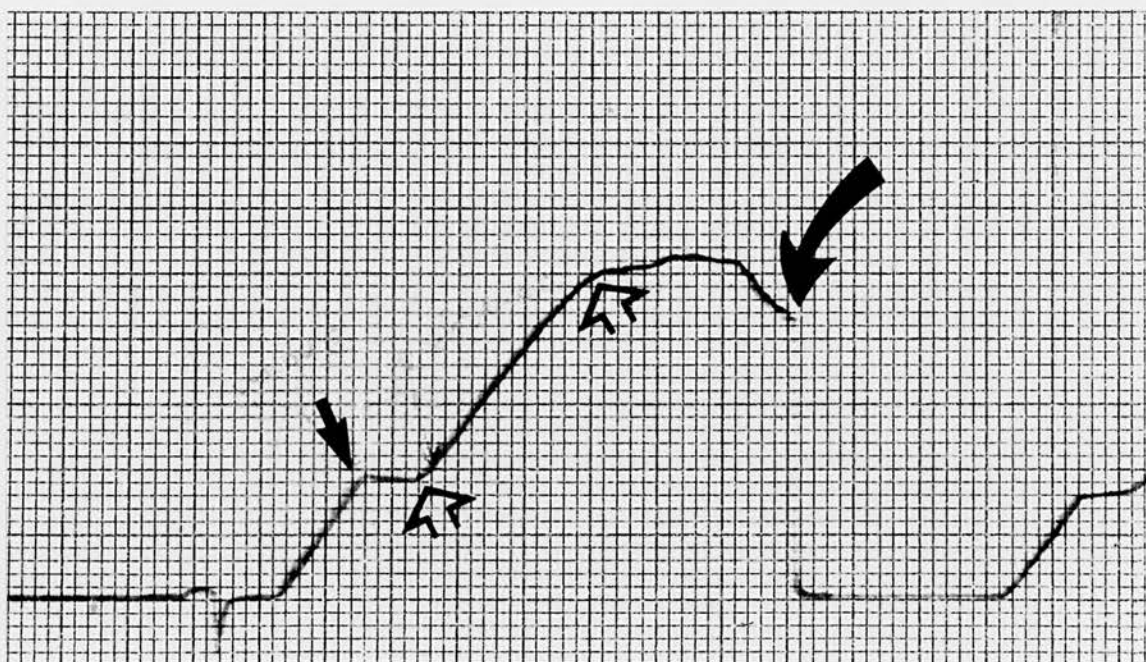


Figure 4: Recording of flow of semi-solid collagen gel in straight glass tube with 50% constriction. Constant flow is achieved prior to the bolus reaching the constriction (small solid arrow). Flow through constriction produces a further increase (two open arrows) to a new plateau. Extrusion is completed and gel bolus drops (curved arrow).

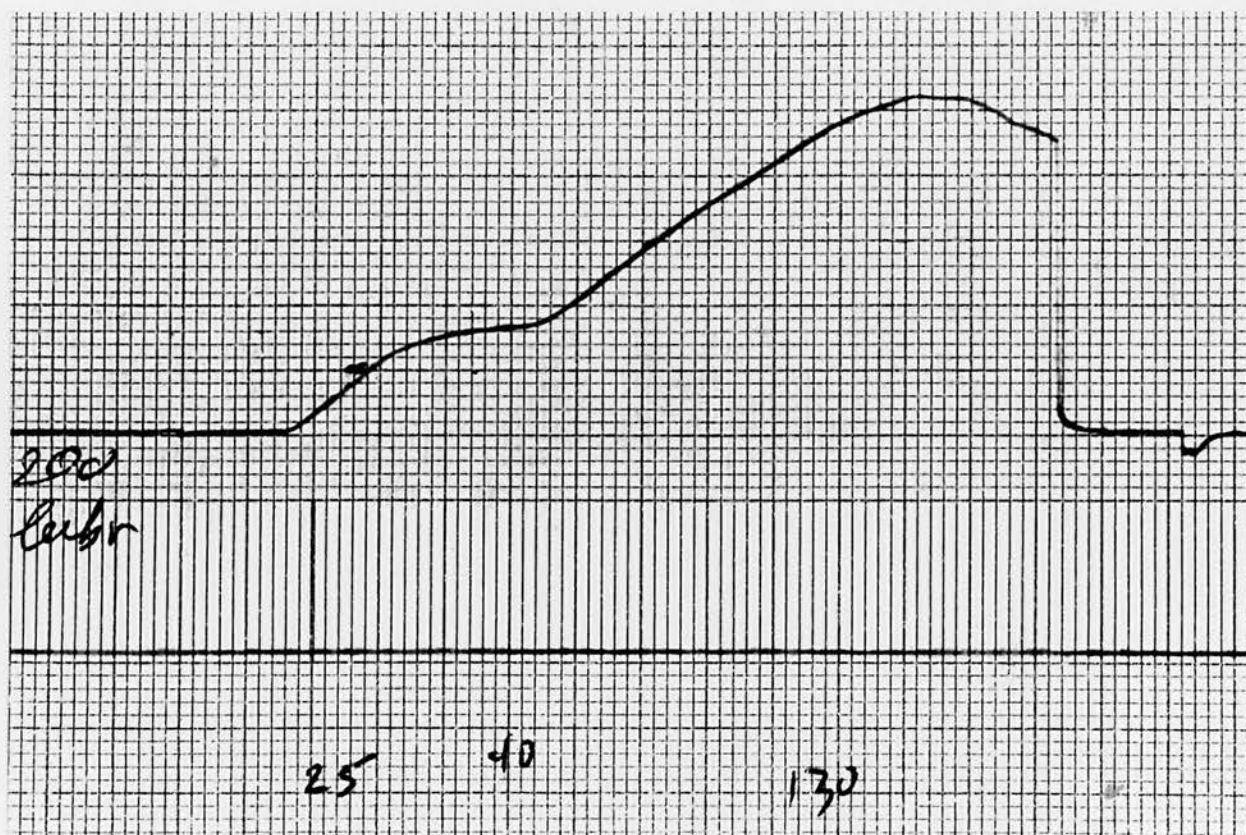


Figure 5: Recording of flow of semi-solid collagen gel in straight glass tube with 50% constriction. Reading taken at faster paper speed; the point at which flow commences is noted (pen mark).

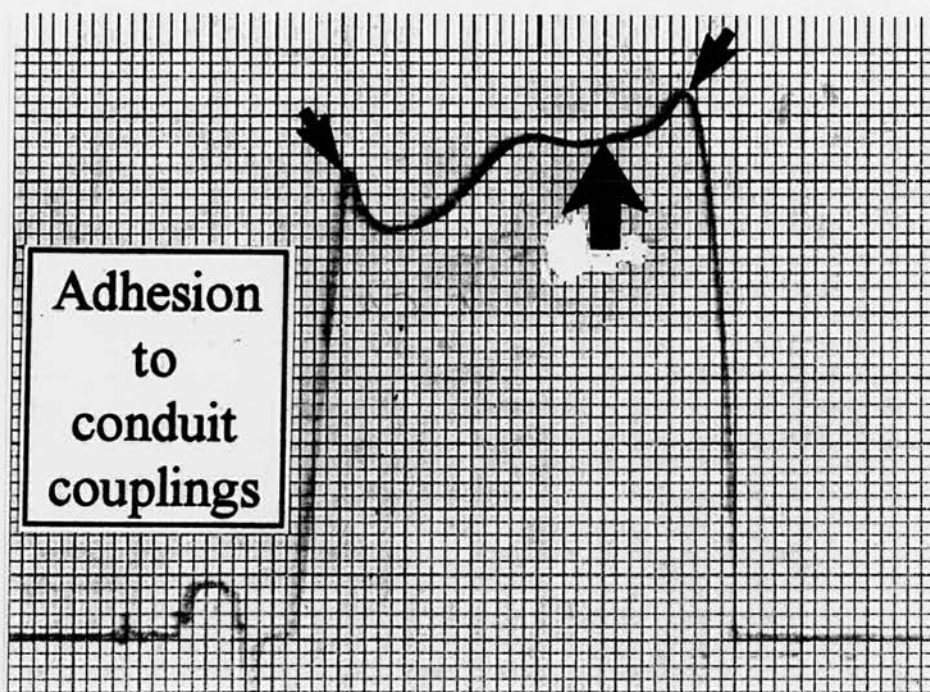


Figure 6: Flow through *unlubricated* glass tube with 90° constriction. The bolus moves after the wall adhesion force is overcome (first small arrow). A new plateau is reached because of the presence of the angulation in the tube (thick arrow). Further increase noted at the end of the extrusion due to adhesion on the tube coupling.

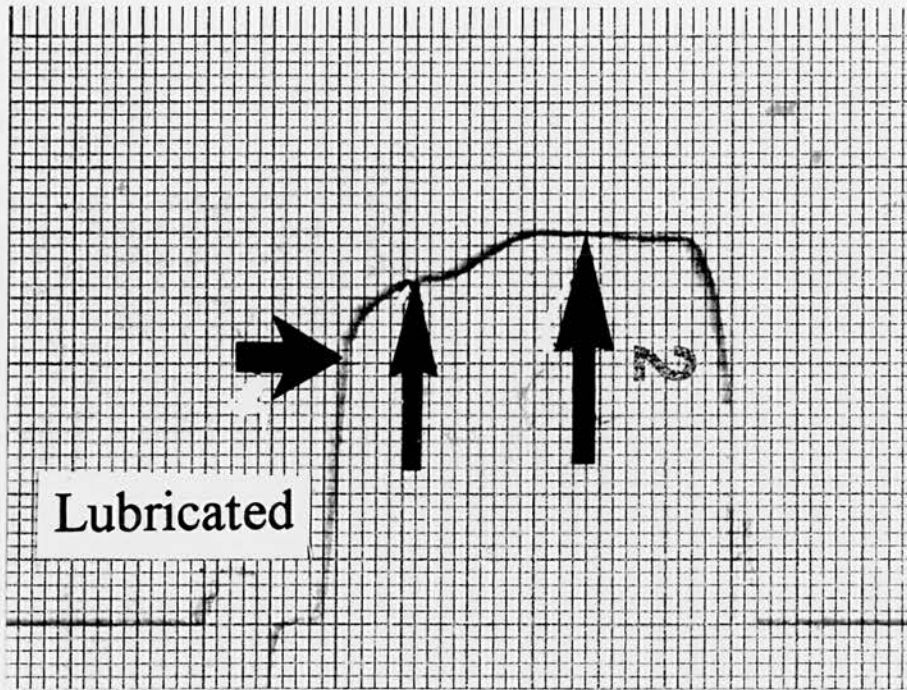


Figure 7: Flow through *lubricated* glass tube with 90° constriction. The bolus moves without measurable wall adhesion (thick arrow), reaching a plateau at constant flow rate (long arrow). A new plateau is reached because of the presence of the angulation in the tube (second long arrow).

Study 3: Rigid Tubes, semi-solid material, plug flow *versus* laminar flow

The experiment was repeated as described in Study 2 above, but the bolus was replaced by two smaller boluses, one coloured red and the other undyed (Figure 11). This was designed to determine whether, at the flow rates studied, the material flowed in a “laminar” or “plug” flow manner.

Results

The pressure exerted on the bowel under the cuff was directly proportional to cuff inflation pressure. The holdback pressure when water was infused into the bowel varied directly with cuff inflation pressure (Figure 8). There was no difference between angulation of 180° and 90° (unpaired t-test, $p=0.93$). Semi-solid material was retained at lower cuff pressures than for water. At 180° there was a linear relationship between cuff and holdback pressures ($r^2= 1.00$). Angulation of 90° improved retention by 100% at low cuff pressures and >300% at 50 mmHg. The bowel ruptured above intraluminal pressure of 150 mmHg (Figure 9).

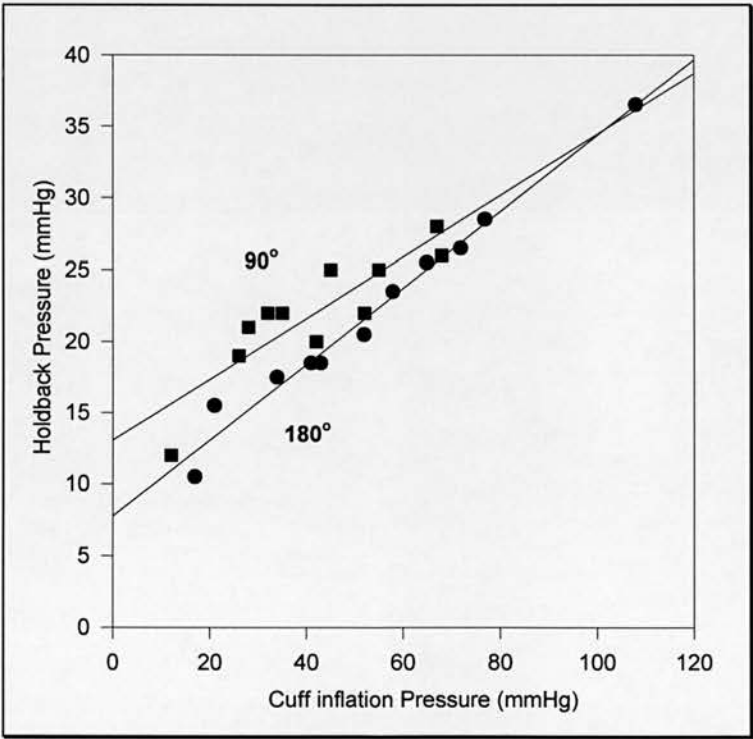


Figure 8: Holdback pressure for water in Bowel at 90° and 180° angulation. Circular cuff Sphincter.

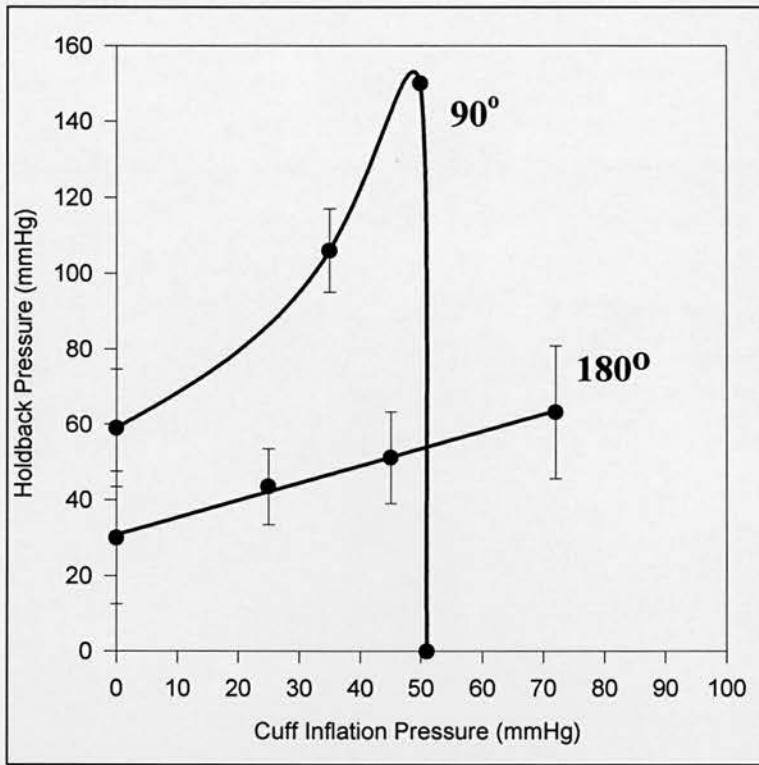


Figure 9: Holdback pressure for semi-solid in Bowel at 90° and 180° angulation. Circular cuff Sphincter.

Flow characteristics of the semi-solid material in the glass tubes are shown in Figure 10 to Figure 11. For each of the tubes, pressure required to move the bolus increased with flow rate. The 50% constriction required approximately 80 mmHg extra pressure to achieve flow whereas the 90° bend needed between 8 and 25 mmHg.

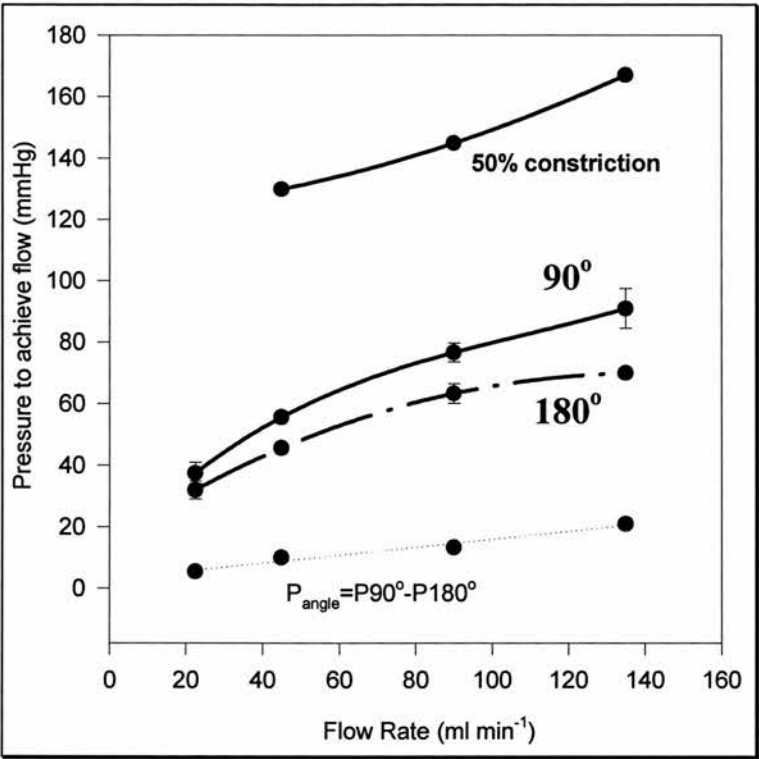


Figure 10: Pressure to drive semisolid material through three glass tubes at different flow rates.

The material exhibited “plug flow” characteristics in each tube at flow rates between 20 and 120 ml/min (3 to 20 cm/min). There was no intrusion of any of the red compound into the colourless at any time to indicate laminar flow (Figure 11).

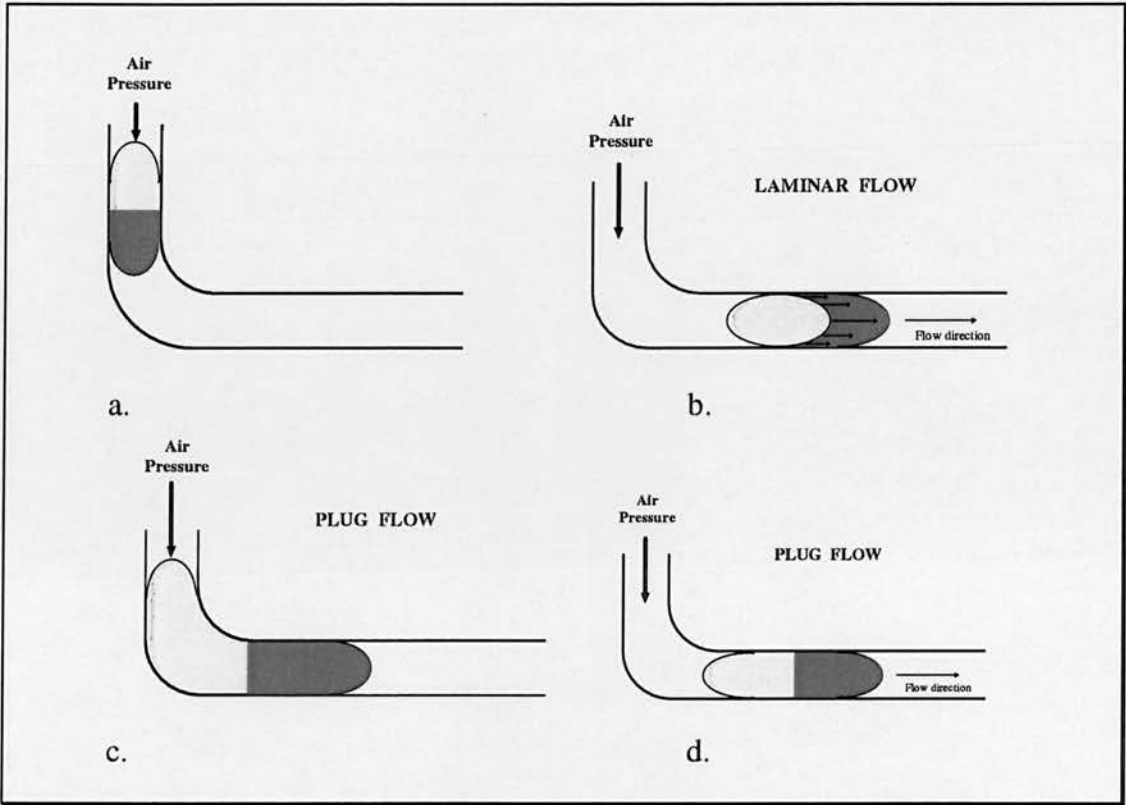


Figure 11: Experiment to determine flow mode of the collagen gel faecal substitute. If flow was laminar, the first bolus of the material would intrude into the second (b.). If the material exhibited “plug flow” characteristics, the two boluses would remain separate (c. , d.). “Plug flow” was exhibited at all gel flow rates studied.

Discussion

The evidence as to whether anorectal angulation is important in maintaining continence is conflicting. Although an obtuse angle is found in patients with idiopathic faecal incontinence⁹, the success of the postanal repair operation^{2,8} which was designed to recreate the acute anorectal angle without affecting anal pressure³, does not correlate with the degree of anorectal angulation achieved¹⁷⁻¹⁹. Further doubt has been cast on the rôle of angulation in creating a flap valve, when it was observed radiologically that the anterior rectal wall did not make contact with the top of the anal canal during the Val-Salva manoeuvre¹². Despite this, it is recognised clinically that patients who have a divided sphincter and poor anal canal tone but a preserved puborectalis and anorectal angle can be remarkably continent, although unable to avert the call to stool.

The present study has shown that to retain liquids in excised bowel required a mucosal seal in which the pressure was greater or equal to intrareservoir pressure, irrespective of angulation. For semi-solids, however, the situation was different: angulation of the bowel improved retention of semi-solids at all occlusion pressures between 0 and 50 mmHg.

Tests to determine the physical properties of faeces^{15,20,21} have shown that they vary considerably in viscosity^{15,21}, hardness and consistency²⁰. The semi-solid gel suspension was chosen because it is a homogeneous substance whose physical properties (density and viscosity) are comparable to those reported for soft faeces¹⁵. On inspection, it had the appearance of soft, well formed stool.

Glass tubes were used to examine the dynamics of flow of the semi-solid material. The minor discrepancy of the shape of the tube at cross section at the apex of the tube was mathematically proven to be negligible (see **Appendix 1**). Flow around a 90° bend without a constriction required extra pressure, while flow through a 50% constriction required even greater pressure, thus both a bend and narrowing in

a rigid tube introduced resistance to flow for the semi-solid. Detailed theoretical analysis of flow through bends is lacking²² and is presented in **Appendix 1**; bends can be thought of as an equivalent length L_{eq} of rigid tubing²³ which introduce an additional frictional force as if an extra length of tubing equal to L_{eq} were interposed. The value of L_{eq} for a 90° angled tube similar in diameter to the human anorectum is 180 cm²³. L_{eq} for a flexible tube may be even greater than that for a rigid tube²⁴.

Although our *in-vitro* models did not attempt to replicate the complexities of the dynamic pressure/volume and angulation changes in the anorectum, we have demonstrated that to retain a semi-solid resembling soft faeces in a tube it is not necessary to seal it. The requirement is that the resistance to flow be equal to or greater than the force tending to move it. Thus, by extrapolation, semi-solid material in the rectum does not need a flap valve to keep it from moving into the anal canal. It would appear that angulation or constriction alone would provide sufficient resistance to prevent movement, even when the rectum is subjected to a minor degree of external pressure. With higher degrees of intra-abdominal or peristaltic pressure, both angulation and occlusion pressure require to be enhanced. The opposite effect, i.e. reduction of resistance to flow by anorectal angle becoming more obtuse and opening of the anal sphincter, occurs during simulated defaecation as observed during proctography^{11,25-27}.

The mechanism for the control of fluid is different; liquids flow easily round bends and require a complete seal to contain them in a tube. For a sphincter to provide a liquid seal the intraluminal pressure must be equal to or greater than the pressure on the liquid. In the Val-Salva study¹², liquid barium filled the rectum and it was observed that the seal was maintained by contraction of the anal sphincter muscles alone. The data from the present study suggests that if semi-solid contrast had been used, there may have been no requirement for the sphincter muscles to respond so vigorously.

Continence to liquid stool is explicable in terms of a delicate balance of pressures. When that balance is disturbed, for example by liquid stool distending the

rectum with increasing intrarectal pressure, then leakage will occur unless sphincter pressure can match rectal pressure. Where damage to the sphincter prevents the creation of an effective pressure barrier, then there will be incontinence to liquid but not necessarily solid stool. It is recognized that there is periodic relaxation of the internal sphincter muscle to allow sampling of rectal contents^{28,29}. The preservation of angulation between the rectum and anal canal probably allows this to occur safely, retaining semi-solids and solids within the rectal ampulla while gas and liquid flow into the upper anal canal.

Our findings may also explain the lack of correlation between angle and success of the postanal repair operation¹⁷⁻¹⁹. In particular, the observation that a 50% stenosis creates more resistance to flow than a 90° angulation suggests that an operation which produces a relative stenosis may also improve continence for formed motions. Therefore, either the creation of stenosis, or the recreation of angle or both would be beneficial in preventing the flow of semi-solids. A longer anal canal length and a relatively fixed perineum, which would achieve a fixed anorectal angulation, also appear important in the maintenance of continence²⁷.

In conclusion, these *in-vitro* studies confirm that for the retention of semi-solid material, angulation enhances the resistance to flow for any given occlusion pressure, suggesting that angulation does provide a physiological benefit in continence. Angulation, however, provides no benefit in the retention of liquid.

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Chapter 2

***In-vitro* assessment of the anorectal flutter valve theory**

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Introduction

The flutter valve theory was proposed by Edwards and Phillips¹ (See: INTRODUCTION AND HISTORICAL PERSPECTIVE: A Review of the Physiological Fæcal Continence Mechanisms). They suggested that normal continence was due partly to intra-abdominal pressure being transmitted at the level of the levator ani, laterally to the side of the anal canal in the region of the anorectal junction. This theory was considered unlikely by Duthie² and Kerremans³.

A series of simple experiments were conducted *in-vitro* to check the validity of the flutter valve theory.

Materials and Method

The abdominal cavity was simulated by a perspex cylinder with perforated ends on which porcine large intestine was secured in order to simulate the gastrointestinal tract. The “intra-abdominal” pressure was increased by air insufflation through a side port (Figure 1). The intestine was filled with collagen gel simulating faeces (**Appendix 2**) or left empty. The behaviour of the system was observed during the air insufflation with the bowel filled (Figure 2), and repeated with the bowel empty (Figure 3).

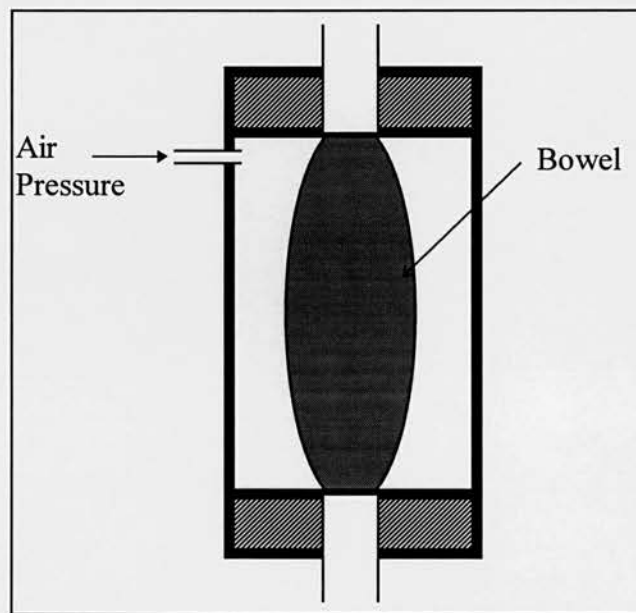


Figure 1: Diagrammatic representation of the *in-vitro* model designed to test the validity of the flutter valve theory.

The air pressure was applied through a modified gas perfusion pressure measuring setup⁴ (Arndorfer 5PS1 Infusion System, Arndorfer Medical Specialists Ltd., Wisconsin).

Results

Intestine filled with collagen gel

The behaviour of the gel is depicted diagrammatically in Figure 2. The observed changes are exaggerated for clarity. Pressure to achieve flow was of the order of 200 mmHg. As the inflation pressure increases, a compressive force is applied on the circumference of the bowel, which tends to constrict it (Figure 2b,c). As the ends of the bowel are open to the exterior (e.g. anal canal) the force causes the material to flow through these orifices to the outside (incontinence).

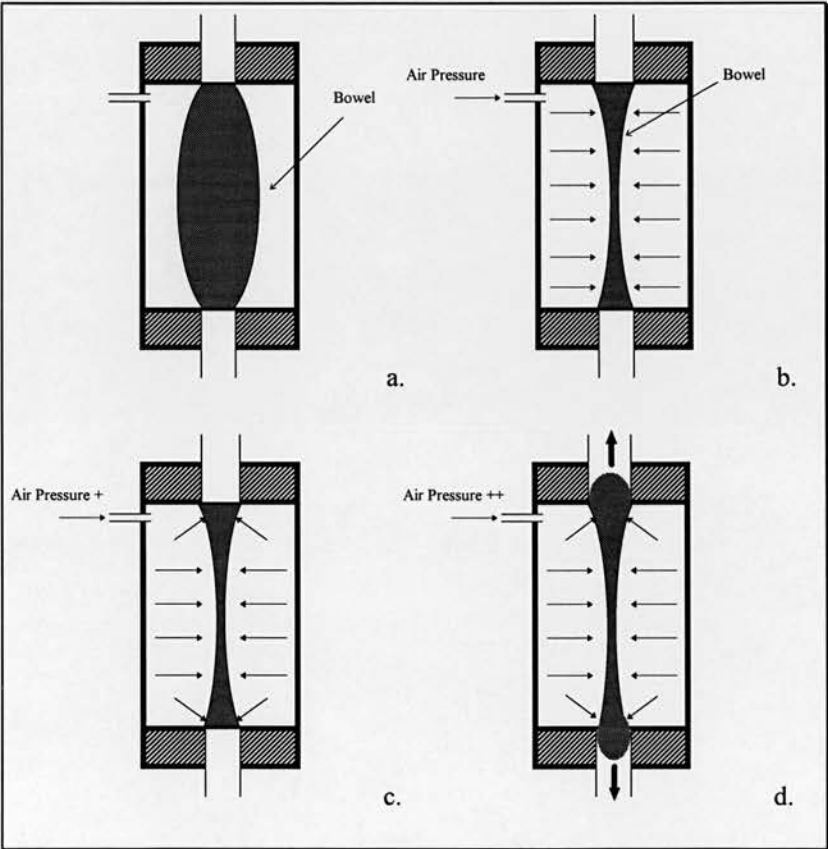


Figure 2: Results of insufflation with bowel filled with gel simulating faeces.

With further increases in pressure, the bowel wall protrudes through the orifices. This is also clearly shown in the next experiment (Figure 3).

Intestine empty

The results of this study are depicted diagrammatically in Figure 3. The empty bowel collapses and the lumen is obliterated progressively almost as soon as the pressure is applied (>25 mmHg). Once all the air is squeezed out, the whole length of the bowel is collapsed. The bowel wall readily protrudes through the two orifices (Figure 3b)

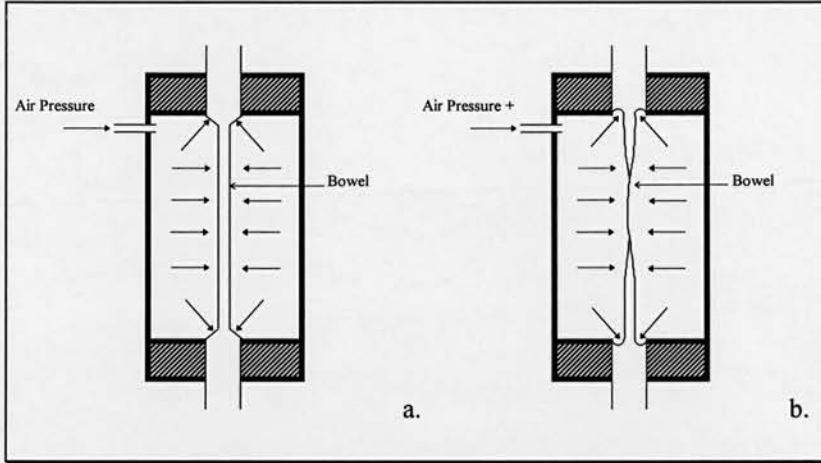


Figure 3: Results of insufflation with the bowel empty.

Discussion

The flutter valve theory was proposed by Edwards and Phillips¹ based on crude radiological methods. They suggested that normal continence was partly due to intra-abdominal pressure being transmitted at the level of the levator ani, laterally to the side of the anal canal in the region of the anorectal junction. The anal canal appears to be an anteroposterior slit¹ radiologically and this pressure could compress it in a way similar to a simple flutter valve (Figure 4). This theory was considered unlikely by Duthie² since although an occlusion was seen radiologically in the anorectal region when the rectum was outlined by barium contrast, puborectalis activity could not be excluded. Kerremans³ also pointed out that the segment described as acting as a flutter valve lies below the levator ani cradle at the level of the puborectalis sling. Radiological observations during the Valsalva manoeuvre

showed that the anterior and posterior rectal walls did not appose one another⁵. Even although the rectal segment examined in their study is above the proposed level of the flutter valve, the fact that increases in the intra-abdominal pressure did not cause the rectal wall to collapse at this level makes it impossible for this pressure to have caused collapse at an even lower level which lies out-with the peritoneal cavity. In addition, rectal pressures were found to be consistently lower than those generated by the anal canal⁵ strengthening the conclusion that continence did not depend on passive 'valvular' mechanisms.

In empirical terms also, the presence of such a valve mechanism is impossible as, in normal subjects without obstructed defæcation, an increase in intra-abdominal pressure is an effective manoeuvre to initiate or complete evacuation.

The flutter valve mechanism, therefore, could not act by increases in intra-abdominal pressure. In addition the flutter valve could not afford protection when the intrarectal pressure rises. Another weakness of this theory is the fact that, in engineering terms, a flap valve can only function if the conduit it would seal is not continuous.

This model was designed to investigate the possibility that a flutter valve mechanism may, indeed, exist. During the experiments pressure measurements were made initially, but they were not analyzed as pressure changed depending on the rate of inflation. In any case the absolute measured pressure is irrelevant in this case, as the model does not serve to show the behaviour of the material, but to observe whether a flutter valve mechanism does exist or not.

The conditions of this experiment cannot represent true changes of intra-abdominal pressure as the abdominal wall is not rigid, but it serves as a simple *in-vitro* approximation. Although the position of the bowel is also simplified, this model proves that a flutter valve mechanism cannot operate in the anorectal region if the bowel contains any material. Increases in ambient pressure would cause the contents of the bowel (be these solid, liquid or gaseous) initially empty. Once emptying is complete, the bowel wall would protrude through the anal orifice. An

increase of intraluminal pressure, however, could still overcome this phenomenon and result in emptying of the luminal contents.

It has, therefore, been proven that the bowel does not act as a biological Heimlich one way valve in the anorectal region.

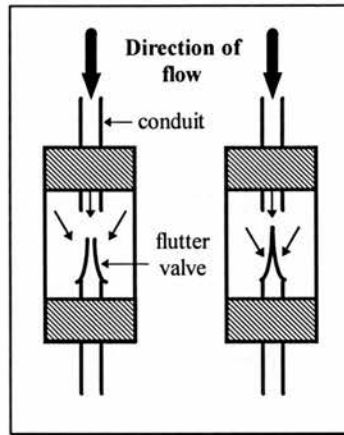


Figure 4: Diagram of a simple flutter valve (Heimlich valve). In order for the flutter mechanism to be effective, the conduit should be discontinuous at the point of the valve.

In engineering terms, the only way that a flutter valve mechanism could exist and protect against increases in the endorectal pressure is either for the lumen to be discontinuous inside a rigid container (Figure 4), or for a segment of intussuscepted bowel to be present interposed between the bowel termination and the outside. Only if this intussusception was fixed and complete, would it enhance holdback of intraluminal contents in response to increases in ambient (intra-abdominal) pressure.

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Chapter 3

Design and evaluation of the Artificial Anal Sphincter Prosthesis (AASP 2000)

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Summary

An artificial anal sphincter¹ was designed to reproduce the normal physiology of the ano-rectum by flattening and angulating the bowel without causing crenation. It was shown in the laboratory that by eliminating crenation, occlusion pressure was evenly distributed without localized high pressure points under the device . Further, the design facilitates the creation of angulation of the bowel with a relatively large area of distribution of the occlusion pressure, allowing the device to be set at lower operating occlusion pressures than that required for circular designs yet still achieve continence(Chapter 1). Each of the components of the device was studied separately and the whole system was assessed in an acute and survival animal model.

Introduction

Attempts have been made to develop a prosthetic anal sphincter but to date these have suffered from many complications. In contrast, urinary incontinence has been successfully treated using an inflatable circular cuff applied to the outer layer of the urethra (see Chapter: Attempts to achieve continence artificially: A Review). A prosthesis of similar circular design has been used for faecal incontinence in animals^{2,3} and humans⁴⁻⁸, but produced intestinal ischaemia at operating pressures which maintain continence^{2,3}. This was probably because the rectum is not “circular” and the application of a circular cuff produced *crenation* of the bowel wall in localized high pressure points within the folds⁹ (see also Chapter 4). These early results did not encourage any further research or development of this device.

It is recognized from our knowledge of the dynamics of flow that it is not necessary to completely seal a tube to prevent flow of a solid/semi-solid if an acute angle is incorporated in the system. Using this principle we have demonstrated in an *in-vitro* study (Chapter 1) that the inclusion of angulation in a tube reduces the occlusion pressure required to hold back solids and semi-solids but is of no benefit for fluids or gas¹⁰.

An artificial anal sphincter¹ is evaluated, which is designed to reproduce the normal physiology of the ano-rectum by flattening and angulating the bowel without causing crenation. This prosthesis is described in a previous Chapter (Attempts to achieve continence artificially: A Review). Detailed analysis of the engineering drawings and development of the device is presented in Appendix 3.

The engineering parameters of the three principal components of the device (the pressure regulating balloon reservoir, the control pump and the sphincter element) and also those of an evolution component (manually operated switch) were studied both *in-vitro* and *in-vivo*. The function of the device was also assessed in acute (Chapter 4) and survival (Chapter 6) experiments in a porcine model. The preliminary assessment in humans is described in Chapter 8.

In an attempt to harmonize and simplify the procedures of licensing medical devices throughout the European Community, the CE marking policy has been introduced. If a device carries the CE mark, it means that the European Community Directives have been followed and the device is likewise approved. In the UK the competent authority for CE marking is the Medical Devices Agency (MDA). Medical devices are classed into Class I, II or III depending on whether they are passive, biologically inactive or biologically active respectively. By definition, Class III includes all self powered devices. Classification of a device in one class allows for automatic approval of modified designs, assuming the changes do not reclassify the device. This device was classified in Class IIb and a design dossier has been submitted for CE approval.

Materials and Methods

Study 1: *In-vitro* assessment

The pressure regulating balloon reservoir

A silicone balloon was used to act as a fluid reservoir and provide the pressure required to drive the system. Two prototypes were studied, one constructed by five and another by six consecutive dips into molten silicone prior to thermal curing (Biosil Ltd.). The balloon was connected to a syringe and inflated with increasing volumes of water, while at the same time the pressure generated inside the balloon was measured by a fluid filled transducer (Baxter Ltd.). The measurements were performed both while injecting and withdrawing water and the results plotted to construct a hysteresis curve. All measurements were repeated five times.

The control pump

This was similar in operation with the AMS 800 unit which is described elsewhere (Attempts to achieve continence artificially: A Review, The Future, Appendix 3).

The shutoff valve

The shutoff valve consisted of a simple piston type valve that could be closed by applying pressure manually on its superior aspect. The valve could be opened by application of transmitted pressure on its inferior surface, by squeezing on the bulb (Figure 1).

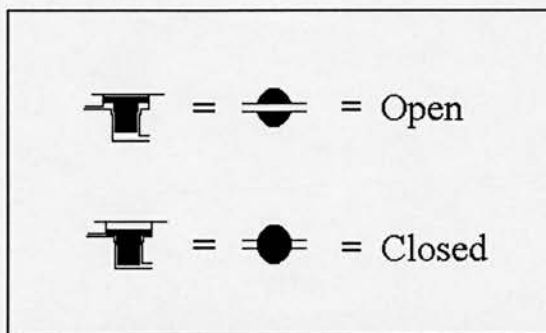


Figure 1: Diagrammatic representation of the shutoff valve in its open (activated) and closed (deactivated) positions.

The pressure required to open the shutoff valve was assessed as follows: the pump case was impaled with a #21 needle connected to a pressure transducer (Baxter Ltd.) so that the pressure generated inside the bulb could be measured while pumping. This pressure is applied to the bottom of the shutoff valve and should lift it off its seat after a critical level is exceeded. The pressure waveform was continuously recorded on a chart recorder (Gould Model 8188-2202-09). The measurements were repeated at a range of pressures applied by the balloon on the shutoff valve.

The vacuum pressure developed in the bulb was also assessed by squeezing the bulb and clamping the expander outlet tube while the shutoff valve was closed. Upon releasing the bulb, a negative pressure is developed which is proportional to the elasticity of the bulb.

Similar measurements were performed on a specimen AMS 800 pump.

The fluid equilibrating resistor

This component consisted of a narrow tube (diameter 0.15-0.2 mm), braze welded inside a stainless steel cuff and held in place inside the pump casing by a Y-shaped steel catch (Figure 2).

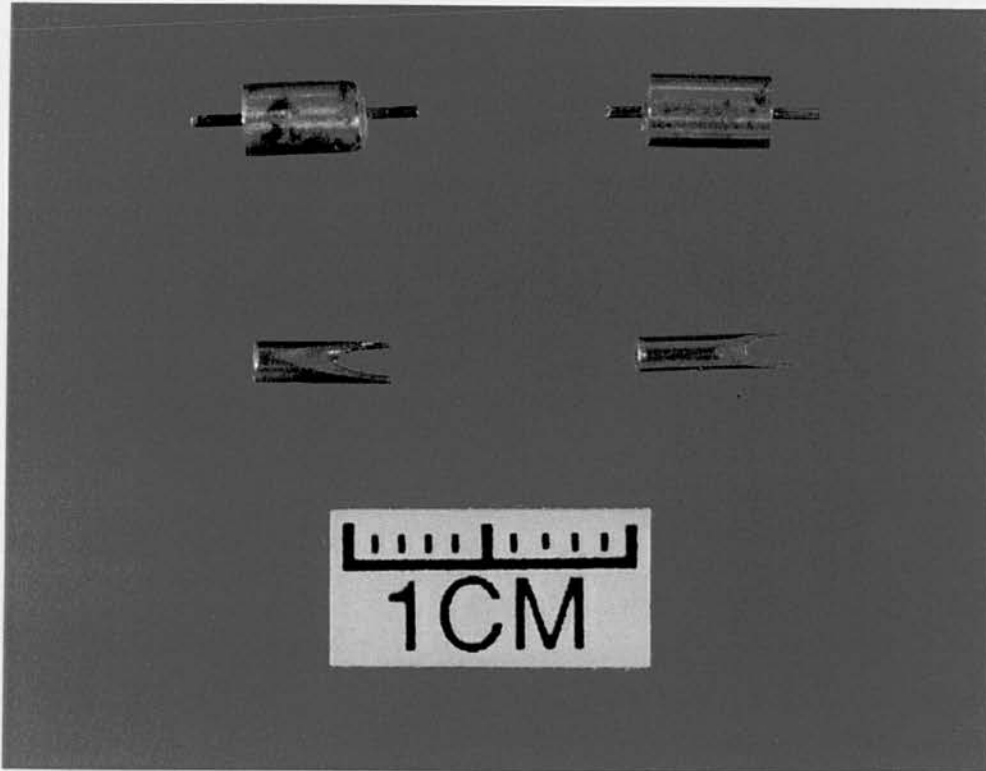


Figure 2: Photograph of the fluid equilibrating resistor and the securing catch. The resistor on the left shows evidence of corrosion (see results section).

Testing was effected in the following ways:

1. The resistor was connected to a variable pressure head and allowed a timed leak. This was repeated for a range of resistor fluid path diameters and at a range of head pressures.
2. The control pump was connected to a variable pressure head and allowed a timed leak. This was repeated for a range of head pressures.
3. The control pump was connected to a variable pressure head and pumped twenty times. The volume of fluid pumped and the time taken to complete the operation were measured. This experiment was repeated for a range of head pressures.

The one way ball valve assembly

The pressure gradient across the one way ball valves was determined by simultaneously recording the pressure during pumping by two transducers placed on either side of the valve. This was achieved by impaling the pump case at appropriate points. Their operation was also checked visually during pumping.

The self sealing injection port

This was assessed visually after impalement and by applying pressure to the bulb with the pump outlets clamped.

The sphincter element

The sphincter element consists of a rectangular expander which comprises two components vulcanized together, interconnected by a large central communication (Figure 3). It is fixed by two straps on to a rectangular silicone gel filled pillow. The distance between these two components (i.e. the effective lumen through stool could pass) is set by using specially designed cylindrical sizors of diameters 20, 22.5, 25 mm (Chapter 6). The bowel is placed between the two components of the device and the expander is connected to the balloon via the control pump.

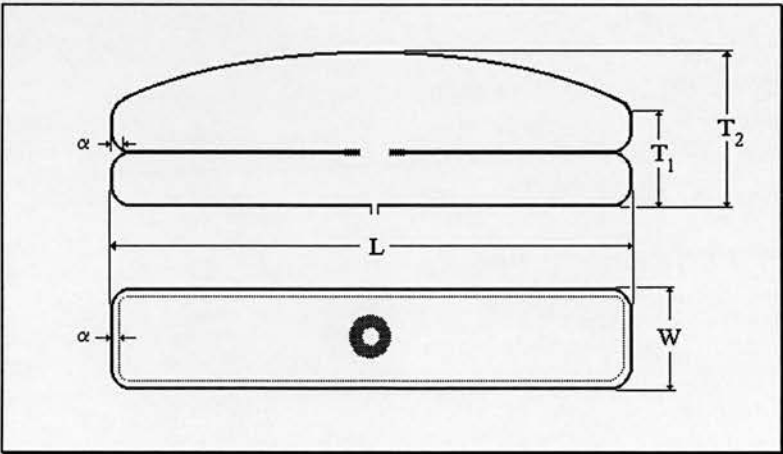


Figure 3: The expander element viewed side on (top drawing) and from above (bottom drawing) to show the central communication between the two components. The linear dimensions are also defined.

Two prototypes were assessed: one with cutout of 1 mm and the other with cutout of 3.5 mm (dimension α in Figure 3). All units subsequently used in the survival animal experiments had a 3.5 mm cutout and length (L) of 55 mm.

The expander was inflated with water to increasing volumes and the pressure generated inside measured. The two prototypes were connected in series and their linear dimensions measured under isobaric conditions (Figure 4) in order to determine the most suitable geometry of the device.

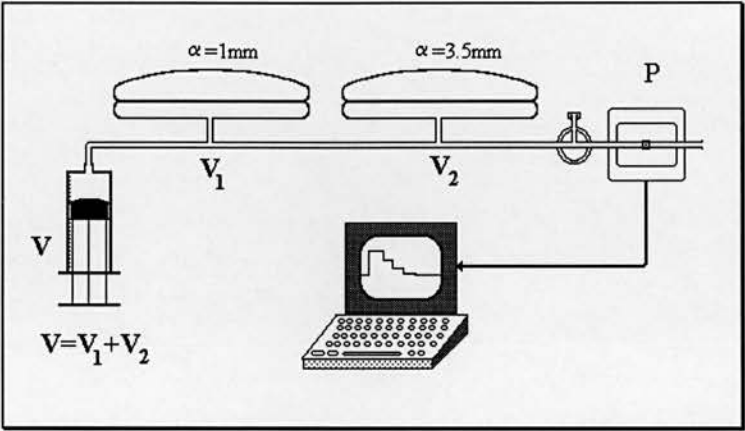


Figure 4: Experimental set up to assess the linear expansion and compliance of the different expander elements.

The pressure-volume relationship of the expander was also studied while it was fixed to the pillow. The lumen was set by using the three specially designed cylindrical sizers described above. The contact angle created by the expander on the pillow was assessed by placing a thin sheet of paper between these two components. Upon progressive inflation of the expander, the paper assumed the contour of the expander and the angle between the tangent at each side of the expander was measured with a goniometer.

Pressure transmission onto the pillow was studied by impaling the pillow and measuring the pressure inside it with progressive inflation of the expander.

All the above measurements were performed at three predetermined distances between these two components (20 mm, 22.5 mm, 25 mm) set by the previously described cylindrical sizers. In addition, the pressure-volume relationship was performed on the expander alone without it being fixed to the pillow. One expander was used for the angle measurements and two for all other experiments.

The pressure distribution under the expander was measured with the straps set at 22.5 mm and the expander inflated to 40 mmHg. Thawed porcine bowel was placed between the expander and pillow and the pressure profile was measured at the midpoint of the expander and also at three points in the periphery by a catheter tipped microtransducer (Gaeltec Ltd., Model CTU1) using the station pullthrough technique.

The holdback properties of this device were assessed using the same methodology used for the circular sphincter as described in Chapter 1. The simulated faecal material developed (Appendix 2) was also used for this experiment.

The manually operated switch

Due to the frequent malfunctions of the control pump shutoff valve and fluid equilibrating resistor, a manually operated switch was employed in the latter animals in an attempt to solve these problems. It consisted of a commercially available pipe occluding unit (clip) placed around a length of silicone tube (Figure 5) and then encapsulated. The whole unit was autoclaved prior to implantation. This unit was designed in an attempt to overcome the problems caused by the control pump in order to conclude the cycle of the experiments. It was not developed any further.

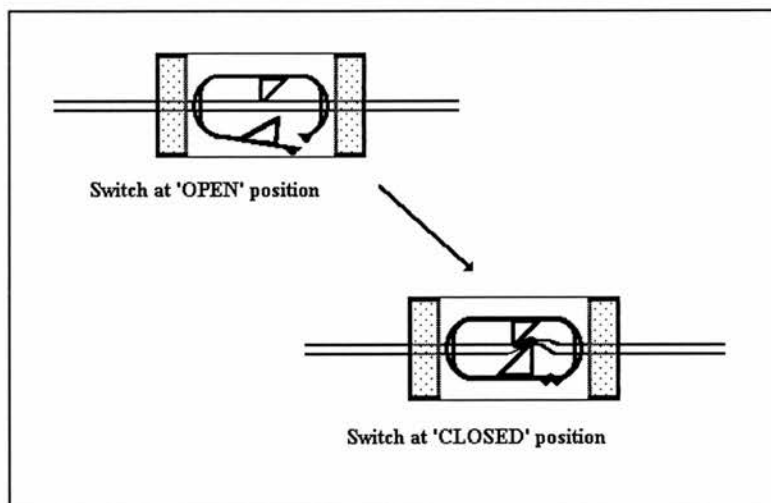


Figure 5: The manually operated hydraulic switch.

One of these switches could be implanted in series between the balloon and the pump in order to ensure reliable deactivation of the system. The other could be connected in parallel with the pump to bypass a potentially blocked resistor. This would provide a manually activated/deactivated shunt pathway allowing operation of the sphincter even if the resistor was blocked (Figure 6).

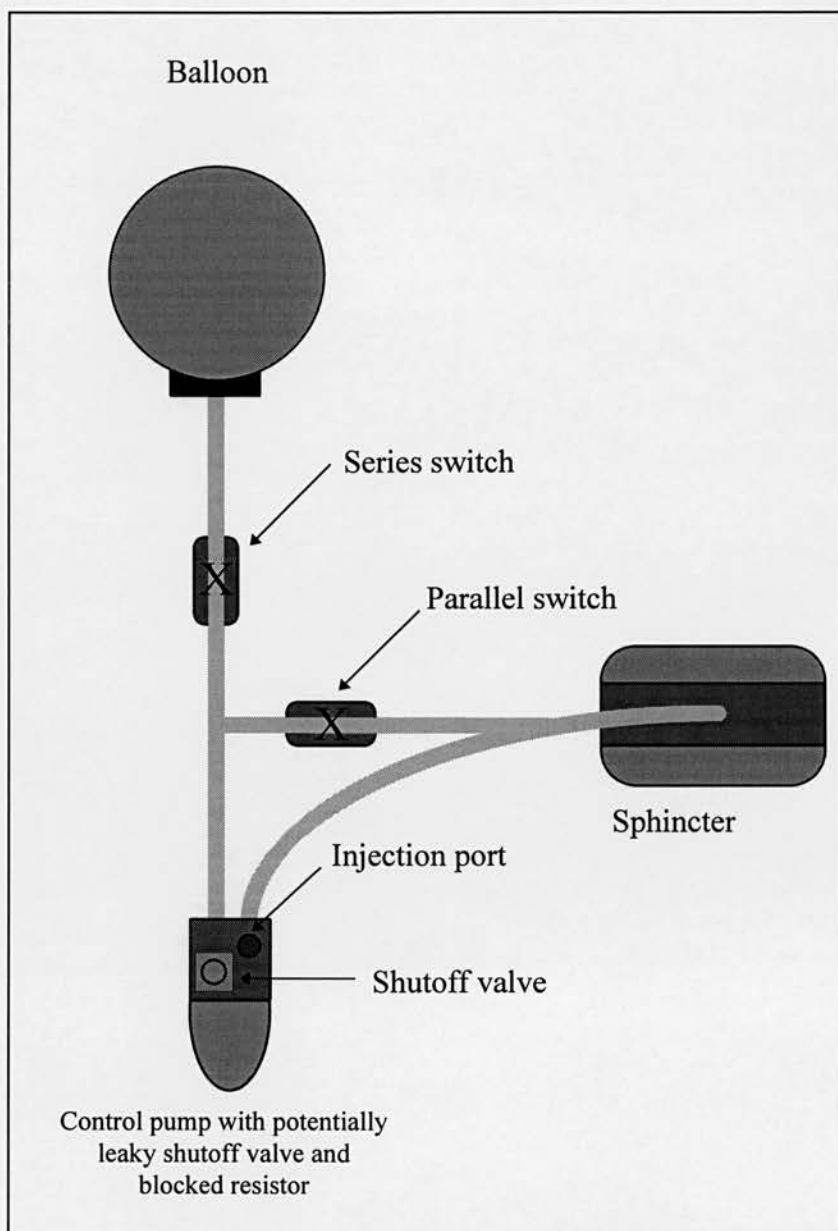


Figure 6: Connections of the two manually activated hydraulic switches.

Study 2: *In-vivo* assessment

The pressure regulating balloon reservoir

The “six-dip” balloon was used in the *in-vivo* experiments. Pressure-volume relationships of the balloons were performed at implantation in 15 of the survival

animals and also in 12 animals just prior to termination with the balloon *in situ* in order to assess the effect of long term implantation.

The control pump

The function of the control pump was assessed visually prior to implantation. The cause of complications or malfunctions was assessed as far as possible by manipulation of the pump and also by impaling the self sealing port percutaneously under general anaesthesia.

The sphincter element

The 55 mm expander with a 3.5 mm cutout was used in the *in-vivo* experiments. The expander was separated from the pillow by the 22.5 mm sizer in all the implanted animals. Pressure-volume relationships of the sphincters were performed at implantation in 14 of the survival animals and also in 11 animals just prior to termination with the sphincter *in situ* in order to assess the effect of long term implantation.

The pressure-volume of the whole system was also studied at implantation in 13 animals and at termination in seven.

The pressure profile under the center point of the expander at increasing inflation pressures was also measured in the animals at implantation. It was not possible to repeat this measurement at termination due to the development of a capsule around the sphincter.

The manually operated switch

The switches were operated at approximately two weeks post-operatively once the tissue oedema resolved. Their appearance was also checked radiologically when indicated and the pressure inside the casing was assessed by impaling the switch percutaneously under a general anaesthetic (Chapter 7).

Results

Study 1: In-vitro assessment

The pressure regulating balloon reservoir

The pressure-volume relationship of the balloon prototypes is shown in Figure 7. The plateau pressure of the six dip balloon was approximately 100 mmHg and that of the five dip balloon 72 mmHg. Both curves showed the hysteresis phenomenon.

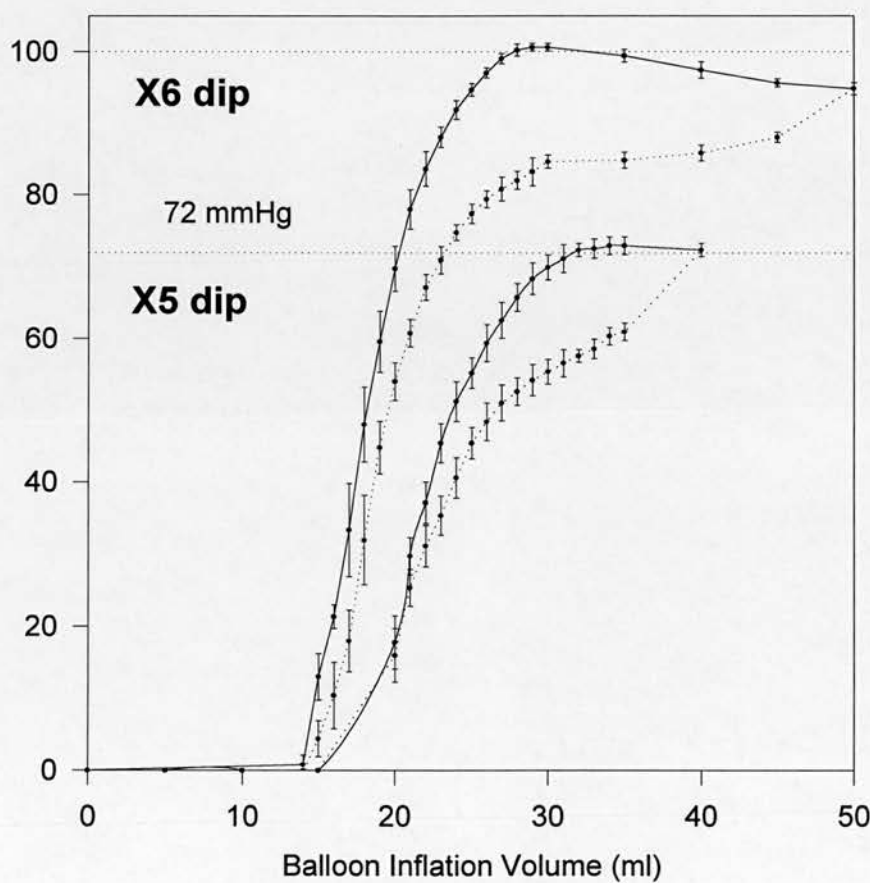


Figure 7: Pressure-Volume relationship of the balloon prototypes. Solid line represents measurements during injection and dotted during withdrawal of fluid.

The control pump

The shutoff valve

The shutoff valve unseating pressure of the AMS pump pre-implantation was 435 mmHg (S.D.=26.6) at 0 mmHg head pressure. When tested after implantation, this was found to be 466 mmHg (S.D.=42) at 0 mmHg head pressure and 418 mmHg (S.D.=54.6) at 100 mmHg head pressure. The differences were not statistically significant between the pre- and two post implantation readings ($p=0.05$ and $p=0.28$) and amongst the two post implantation readings ($p=0.08$).

The mean unseating pressure of all valves tested was 312 mmHg (S.E.M.=98.8) at 0 mmHg head pressure and 325.7 mmHg (S.E.M.=98.4) at 80-100 mmHg head pressures. There was no statistically significant difference between these ($p=0.75$). The results are shown diagrammatically in Figure 8.

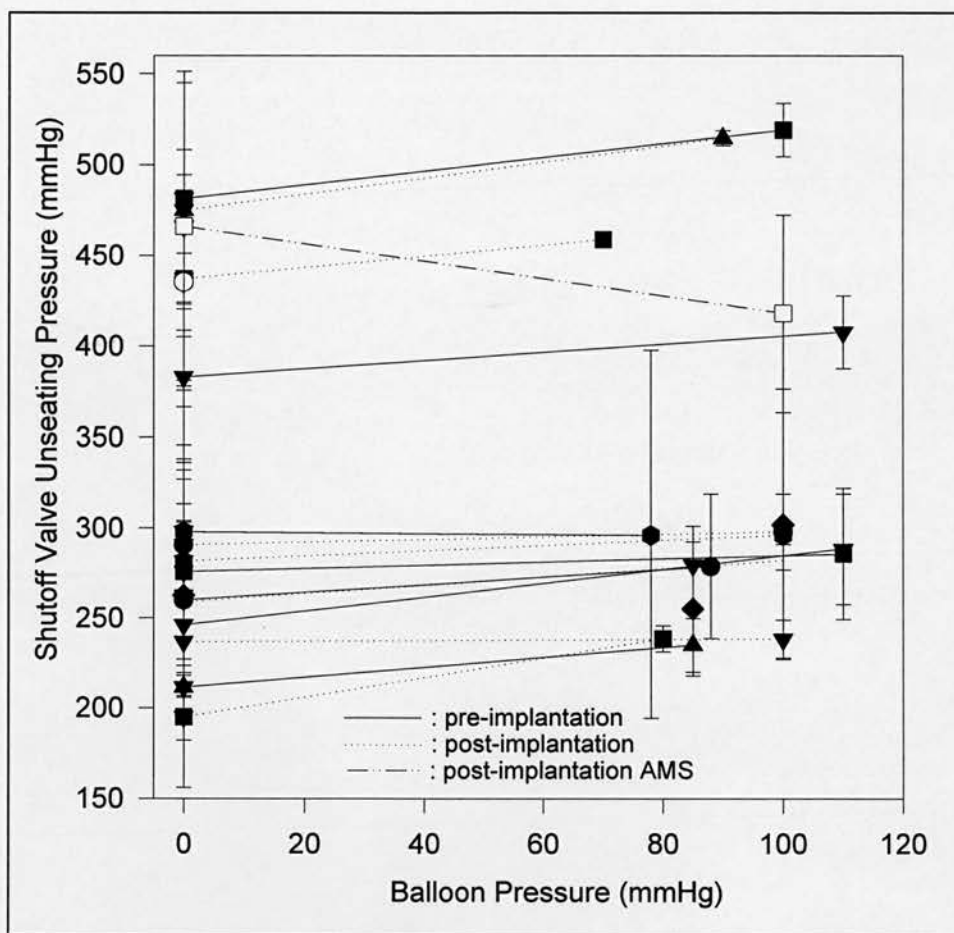


Figure 8: The effect of head pressure (applied by the balloon) on the control pump's shutoff valve unseating pressure.

The operation of the AMS shutoff valve was also much more positive than that of the artificial anal sphincter (Figure 9-Figure 11). This pressure was not dependent on the presence or absence of head pressure (i.e. balloon pressure) in the AMS device, whereas its presence compromised even further the reliability of the AASP device.

The vertical travel of the shutoff valve was assessed radiologically (Chapter 7) and was found to be approximately three times greater in the AMS pump, allowing it to provide a much more positive lock and enhanced reliability.

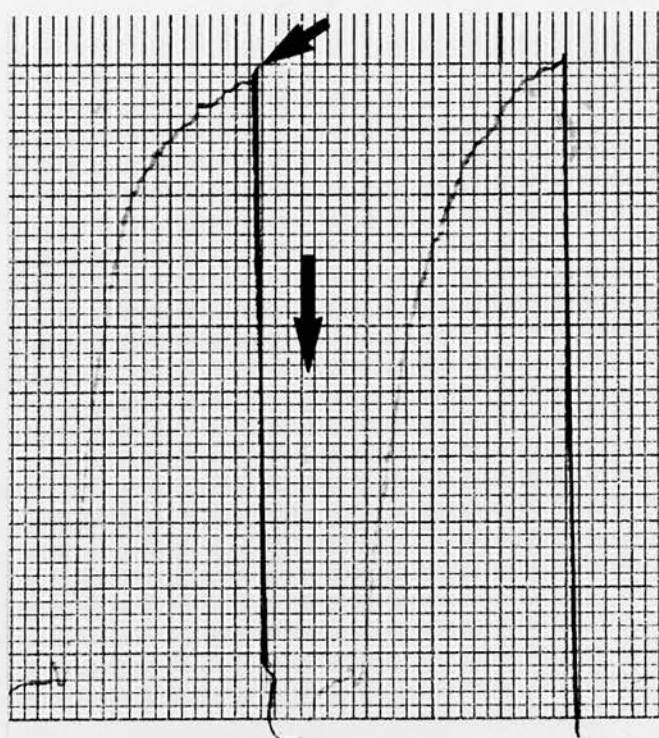


Figure 9: Measurement of unseating pressure of the AMS shutoff valve. Upon squeezing the bulb, the pressure inside it increases up to the point of unseating of the shutoff valve (oblique arrow). It then decreases abruptly (vertical arrow). The trace is the same at head pressures of 0 and 100 mmHg. (Vertical scale = 10 mmHg/mm).

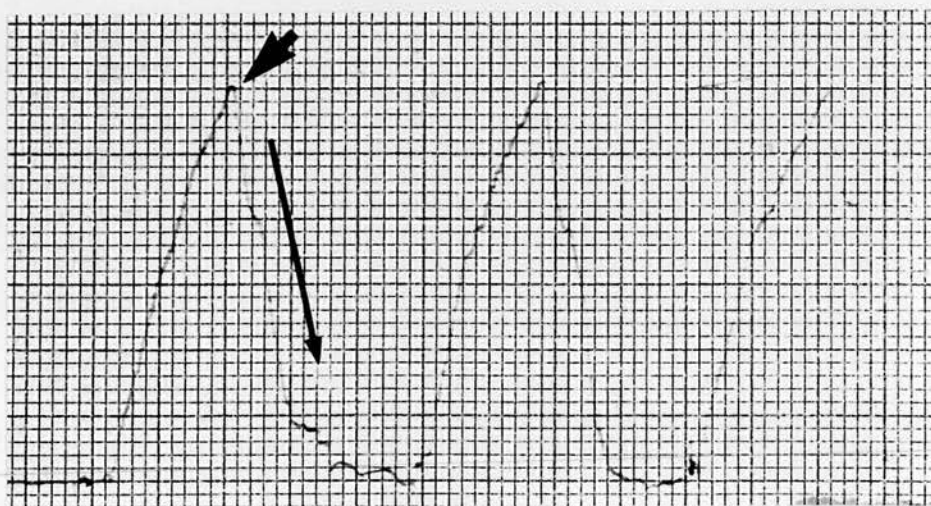


Figure 10: Measurement of unseating pressure of the AASP shutoff valve (no head pressure). Upon squeezing the bulb, the pressure inside it increases up to the point of unseating of the shutoff valve (oblique arrow). It then decreases but not abruptly (downwards arrow) indicating some form of impedance to flow or unreliable shutoff valve opening. (Vertical scale = 10 mmHg/mm).



Figure 11: Measurement of unseating pressure of the AASP shutoff valve with a head pressure of 100 mmHg. Upon squeezing the bulb, the pressure inside it increases up to the plateau before the shutoff valve is fully unseated (oblique arrow). It then decreases but not abruptly (open arrow) indicating that in the presence of head pressure, impedance to flow or unreliable shutoff valve opening is exaggerated. (Vertical scale = 10 mmHg/mm)

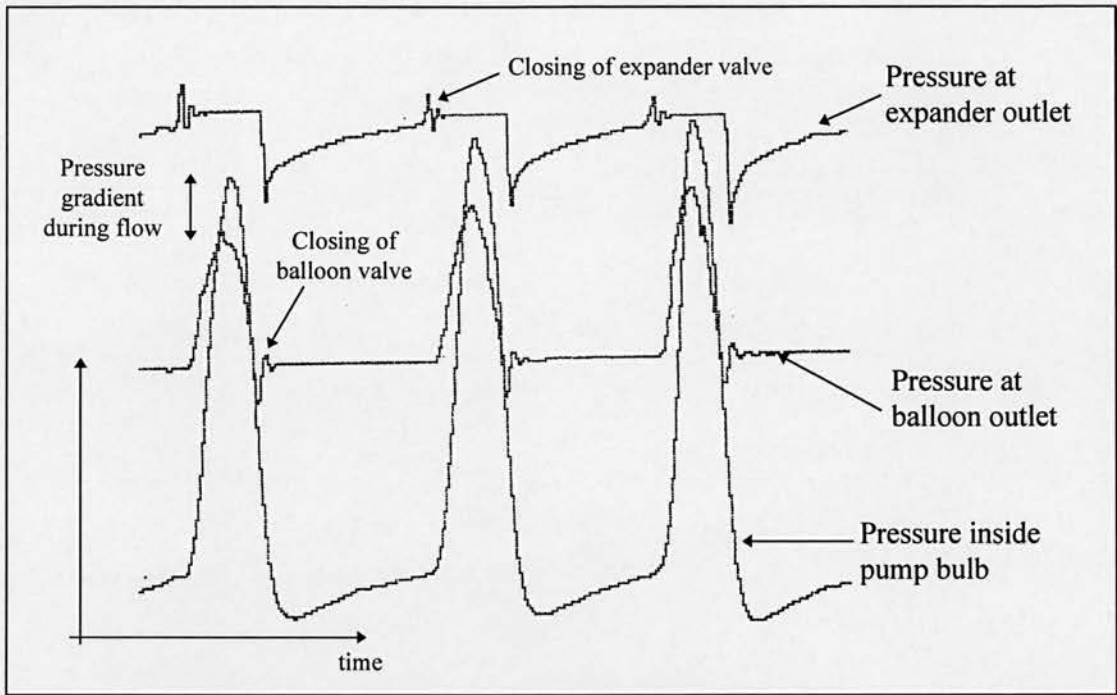


Figure 12: Dynamic measurements at various points inside the pump during its operation.

The appearances in Figure 12 are self explanatory. There is a significant pressure gradient (>25 mmHg) across the fluid outlet pathway on the balloon side of the pump.

The fluid equilibrating resistor

The flow rate increased as the diameter of the resistor lumen increased (Figure 13). The resistor lumen diameter of the prototypes was 0.15-2 mm. This component had the tendency to block.

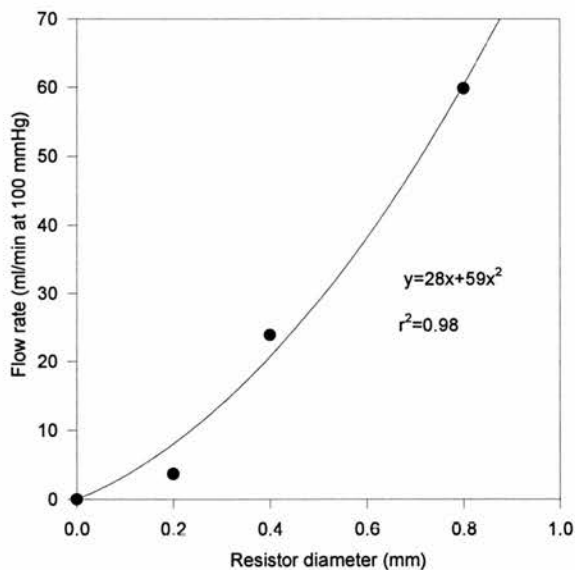


Figure 13: Plot of resistor flow rate versus luminal diameter at 100 mmHg pressure gradient.

The timed liquid flow through three whole pump units is shown in Figure 14. Flow rate is linear and represents the composite leakage of all the fluid pathways across the whole pump (resistor, ball valves, resistor housing).

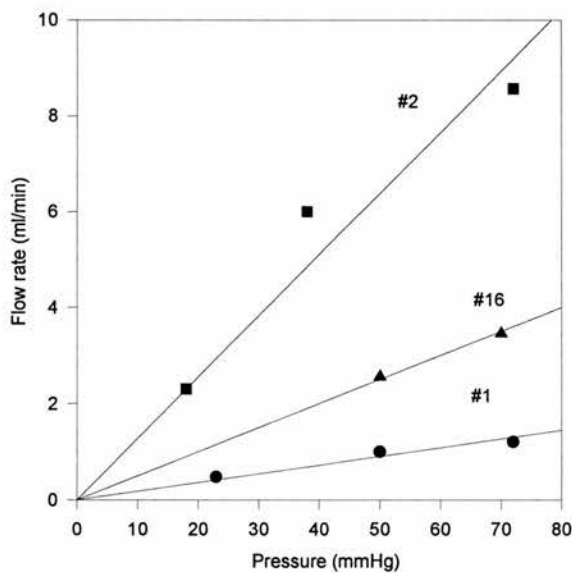


Figure 14: Timed fluid flow through the whole pump as a function of applied head pressure at the balloon side of the pump.

Figure 15 and Figure 16 depict the stroke volume and stroke refill duration of the pump as a function of head pressure.

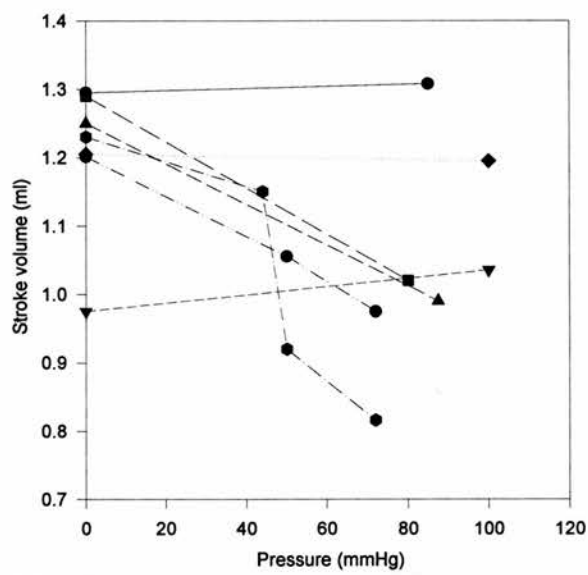


Figure 15: Stroke volume versus applied head pressure for six pumps.

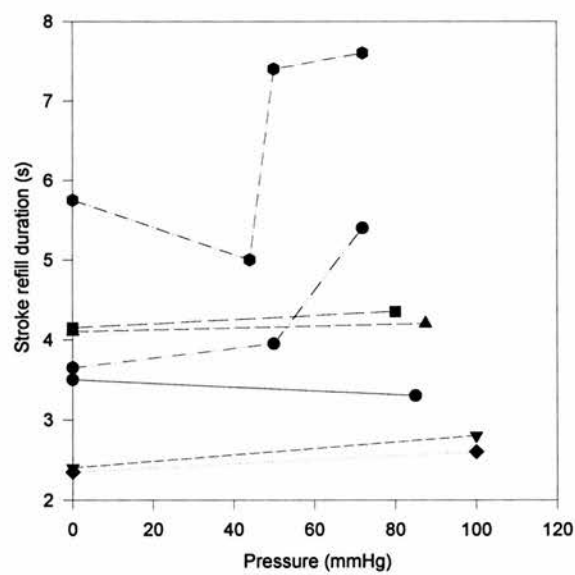


Figure 16: Stroke refill duration versus applied head pressure for six pumps.

The stroke volume decreased significantly from a mean of 1.21 ml (S.D.=0.11) to 1.05 ml (S.D.=0.14) with increasing head pressure ($p<0.02$). This indicates the presence of shunting across the resistor during pumping which slightly compromised pumping efficiency. This effect would become more pronounced with increasing resistor flow rates. Based on these results the critical resistor diameter (or flow rate) which would not compromise pumping efficiency during normal operation can be calculated.

The mean stroke refill time increased from 3.7 sec (S.E.M.=1.16) to 4.7 sec (S.E.M.=1.74). This change was not statistically significant ($p=0.22$). The refill time of the AMS 800 pump bulb was less than 2 sec under all study conditions.

One pump (hexagonal symbol in Figure 15 and Figure 16) had a longer stroke refill time. This was due to a combination of two factors: it had a soft bulb which did not allow effective suction upon pumping and it also had a narrow inlet pathway on the expander side which further impeded fluid flow.

The suction pressure of the AASP 2000 pump bulb with the expander side occluded was studied in six pumps. The bulb created an average suction pressure of 345 mmHg (range = 285-390, S.E.M.=39.5) - Figure 17. The AMS pump specimen studied, created a suction of >500 mmHg.

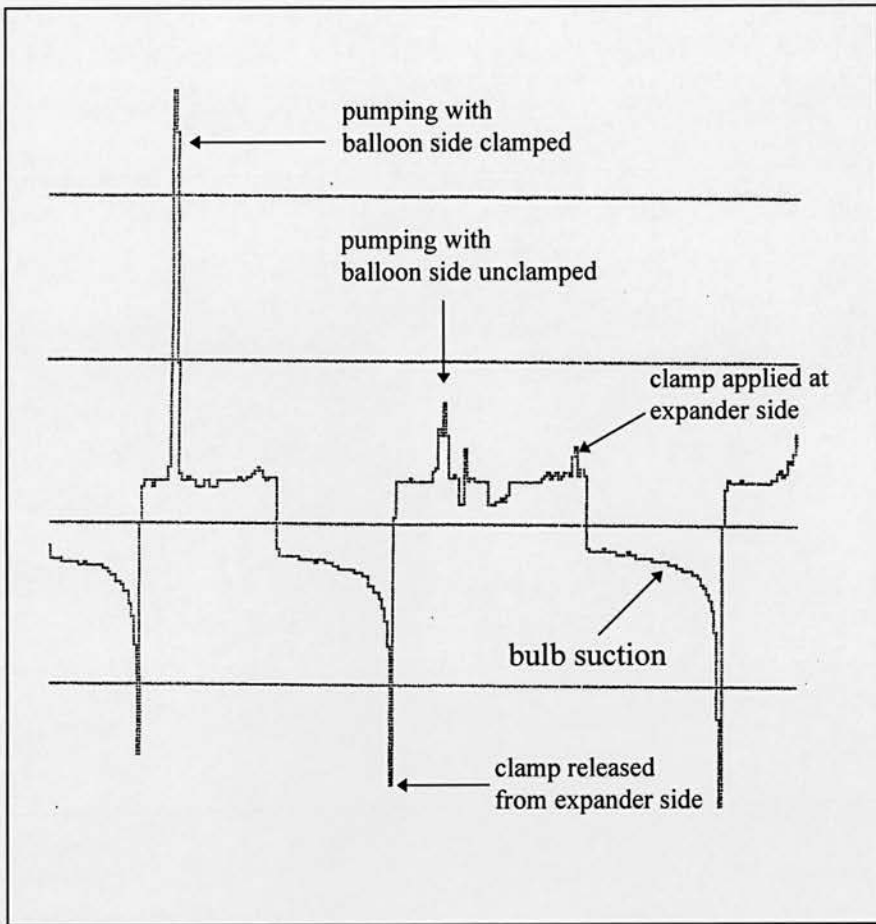


Figure 17: Demonstration of suction created by the pump bulb. The bulb is squeezed and the expander side tubing clamped and the bulb released. The pressure inside the bulb is continuously measured.

The one way ball valve assembly

The pressure gradient across the ball valves was less than 2 mmHg. The valves had a tendency to adhere onto the valve seat during the pumping action. This resulted in pump malfunction due to blockage of the fluid path and could usually be rectified by manually distorting the pump casing until the ball slipped off its seat.

The self sealing injection port

There was invariably visible fluid leakage from the previous puncture holes upon application of pressure onto the bulb with the outlets clamped.

The sphincter element

Figure 18 depicts the inflation pressure-volume relationship of the two prototype expanders (cutout 1 mm and 3.5 mm: dimension α in Figure 3). The inverse of the slope at each point of the curve represents the compliance of the expander. The curve of the unit with $\alpha=3.5$ mm is shifted to the right. Both curves fit third order polynomial regressions as follows:

$\alpha=1\text{mm}$	$\psi = 176 - 55\chi + 5.3\chi^2 - 0.14\chi^3$	$r^2=0.996$
$\alpha=3.5\text{mm}$	$\psi = 76 - 25\chi + 2.3\chi^2 - 0.05\chi^3$	$r^2=0.996$

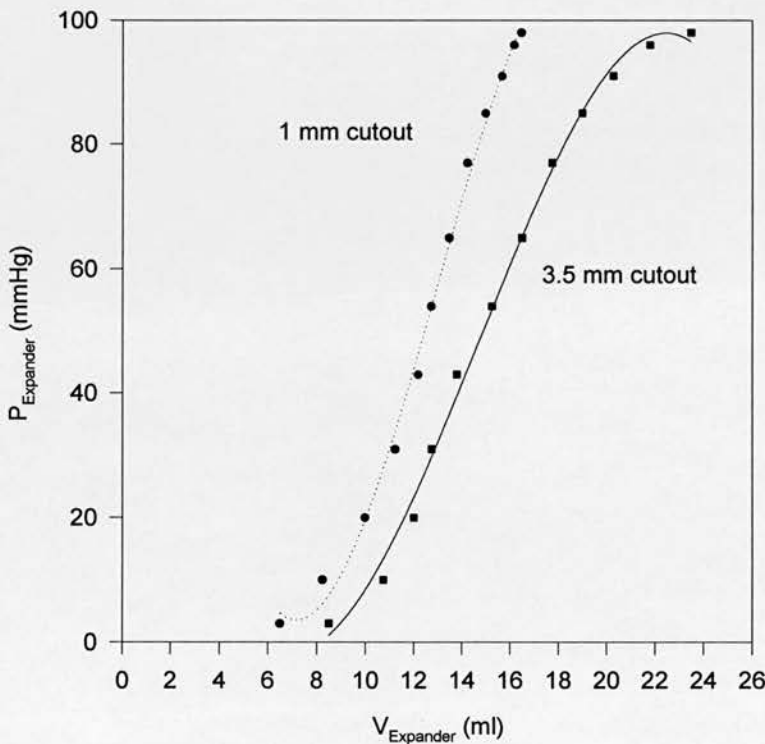


Figure 18: Pressure-volume relationship of the two prototype expanders with cutouts of 1 mm and 3.5 mm.

The above changes are reflected in the total linear elevation of the expander (dimension T_2 in Figure 3). As it can be seen from Figure 19, for each inflation volume, there is more linear expansion of the prototype with a 3.5 mm cutout between the two elements of the expander.

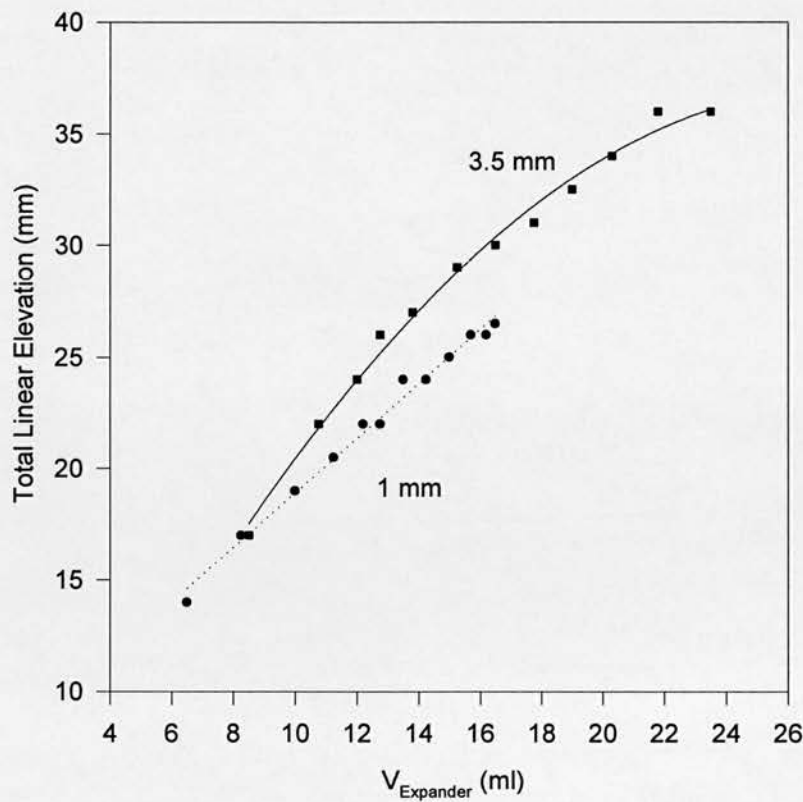


Figure 19: Total linear elevation or expansion (dimension T_2) of the two prototype expanders *versus* inflation volume.

None of the other linear dimensions changed significantly between the two expanders at the range of inflation volumes studied (T_1 : partial linear elevation, L : length, W : width. Defined in Figure 3).

In order to calculate the compliance of the prototypes, certain mathematical manipulations had to be made. The slopes at each point of each curve in Figure 18 are defined by the equations obtained after differentiation of the two polynomial regressions. The following equations are, therefore, obtained:

$$\alpha=1\text{mm} \quad \frac{d\psi}{d\chi} = -55 + 10.6\chi - 0.42\chi^2$$

$$\alpha=3.5\text{mm} \quad \frac{d\psi}{d\chi} = -25 + 4.6\chi - 0.15\chi^2$$

Note that the above equations are valid only for the range of the data that the polynomial regressions show a high correlation (i.e. 6 to 18 ml for $\alpha=1\text{mm}$ and 8 to 24 ml for $\alpha=3.5\text{mm}$). The above equations were solved and the data plotted in Figure 20. As the ψ axis represents Pressure (P) and the χ Volume (V), then $d\psi/d\chi$ represents dP/dV , i.e. the inverse of the compliance. Therefore, by plotting the inverse of the ψ axis data from the plots in Figure 20, we can obtain an estimate of the compliance of the expanders and this is plotted in Figure 21.

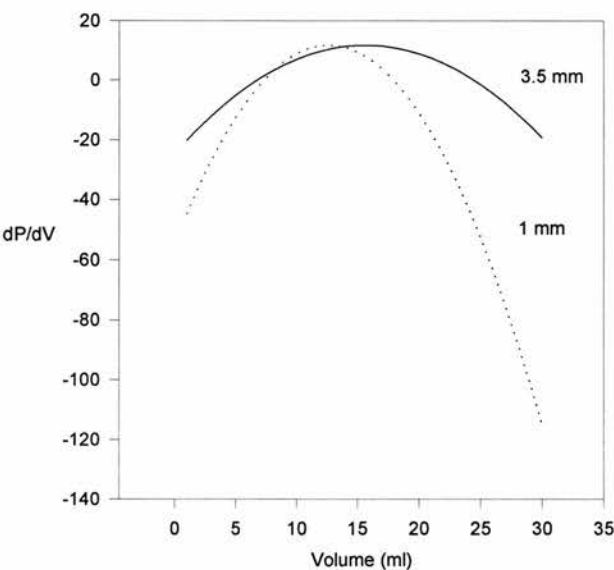


Figure 20: Plot of calculated slope of pressure-volume relationships of the two prototype expanders. This represents the inverse of compliance.

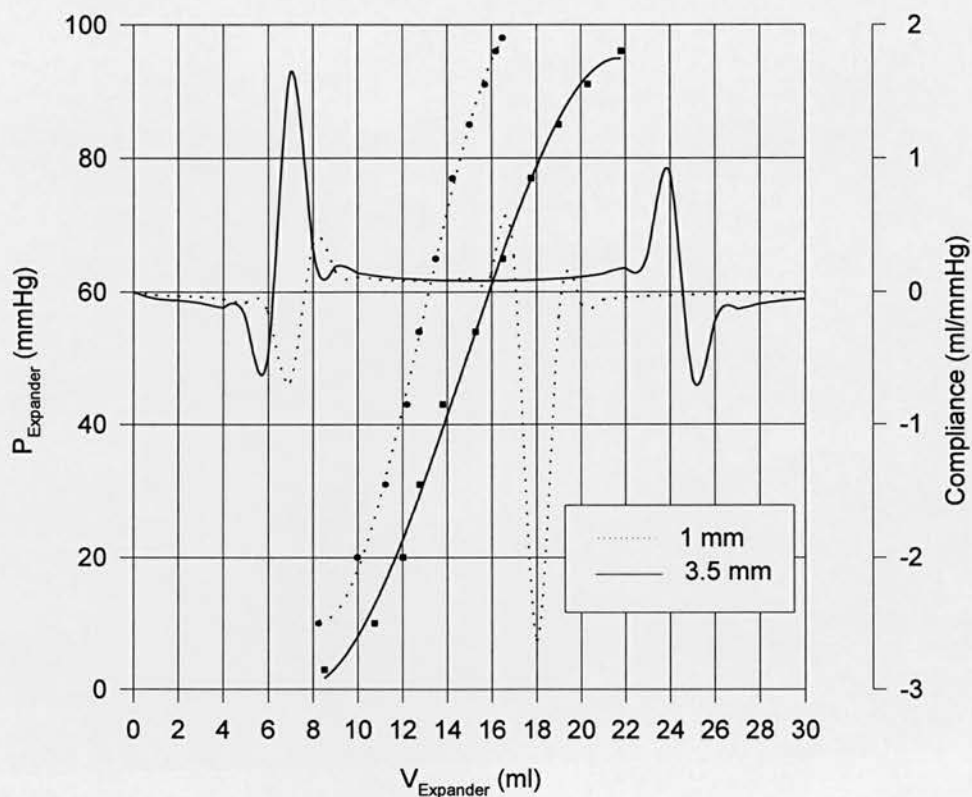


Figure 21: Plots of pressure *versus* volume relationships of the two expander prototypes, superimposed on to the calculated compliance curves.

The calculated compliance is approximately 0.1 ml/mmHg for both expander prototypes but, as can be seen from Figure 21, the increased cutout depth has allowed the device to remain useable with the same compliance over a greater range of inflation volumes (8→22 ml as opposed to 8→15 ml).

Figure 22 and Figure 23 show the pressure-volume relationships of two expanders used in the survival animal experiments at increasing expander/pillow separations from 20 mm to infinity (no pillow). Expander “A” was a prototype where the 3.5 mm cutout was set manually, whereas in expander “B” and subsequent units this dimension was measured and accurately set. As expected, at similar inflation volumes the pressure increases more rapidly with decreasing separation between the two components. The shape of the curves at 22.5 and 25 mm closely match that without the pillow and for expander “B” the two are identical.

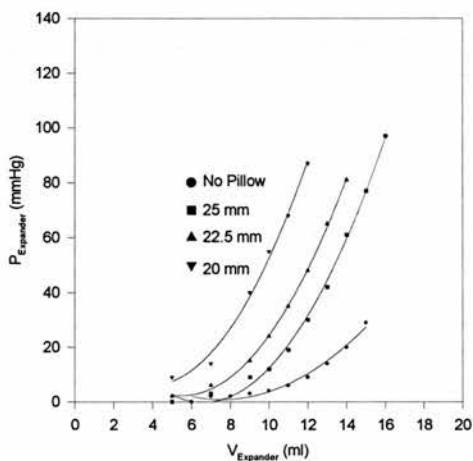


Figure 22: Pressure-volume relationship of expander “A” at increasing pillow separations.

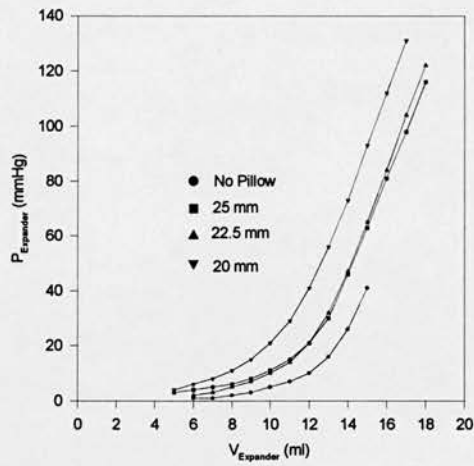


Figure 23: Pressure-volume relationship of expander “B” at increasing pillow separations.

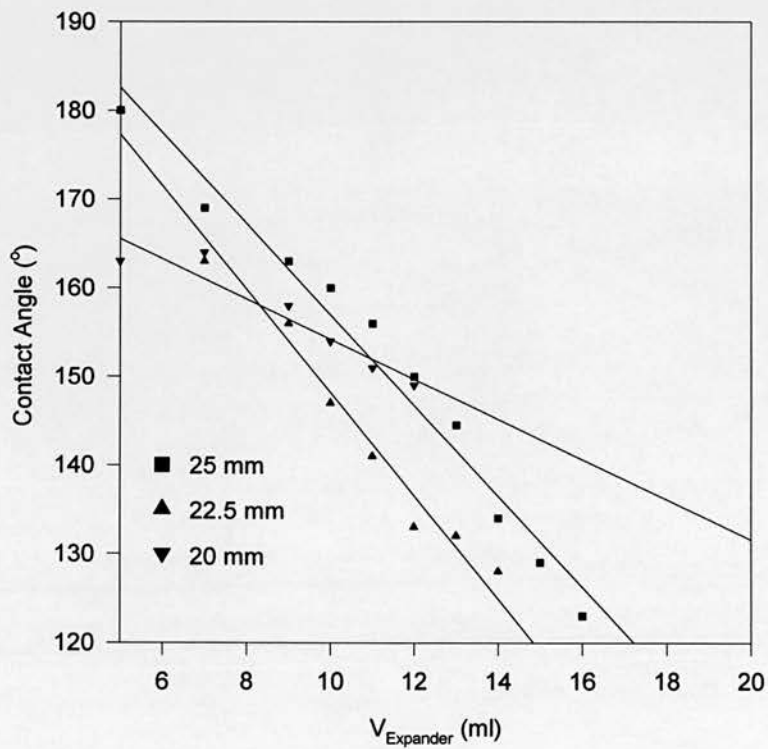


Figure 24: Measurement of contact angle between the expander and pillow at progressive inflation pressures.

At approximately 5 ml inflation volume (22,5 mm and 25 mm original separation), the expander just touches the pillow. The contact angle becomes more acute as the inflation volume (and hence the pressure) is increased. The regressions for the three sets of data are linear with excellent correlation ($r^2= 0.97, 0.98$ and 0.91 for 25 mm, 22.5 mm and 20 mm separation respectively). At inflation volumes greater than 10 ml, more angulation is caused by the device at 22.5 and 25 mm separation than at 20 mm.

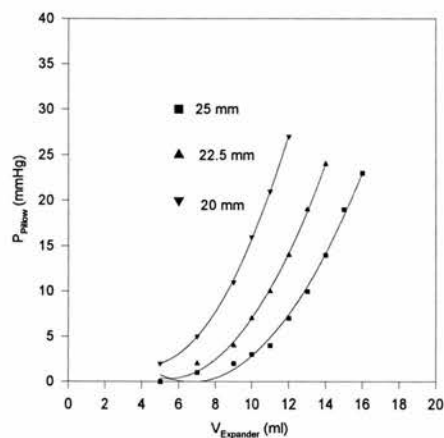


Figure 25: Pressure inside expander “A” as a function of progressive inflation at increasing pillow separations.

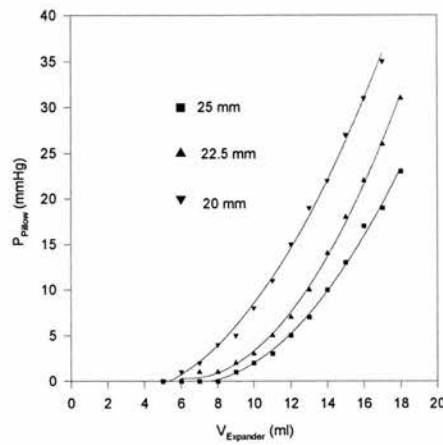


Figure 26: Pressure inside expander “B” as a function of progressive inflation at increasing pillow separations.

Figure 25 and Figure 26 present the results of the measurements of the pressure inside the silicone gel pillow with increasing expander inflation. Pressure inside the pillow began to increase at expander volumes of approximately 5 ml. The increase becomes less pronounced with increasing separation of the expander and pillow. This indicates that some pressure is dissipated by a “hammock” effect created by the pillow.

The following diagram was constructed by generating data by a 3-D curve fitting computer program to interpolate the points between the experimental pressure measurements.

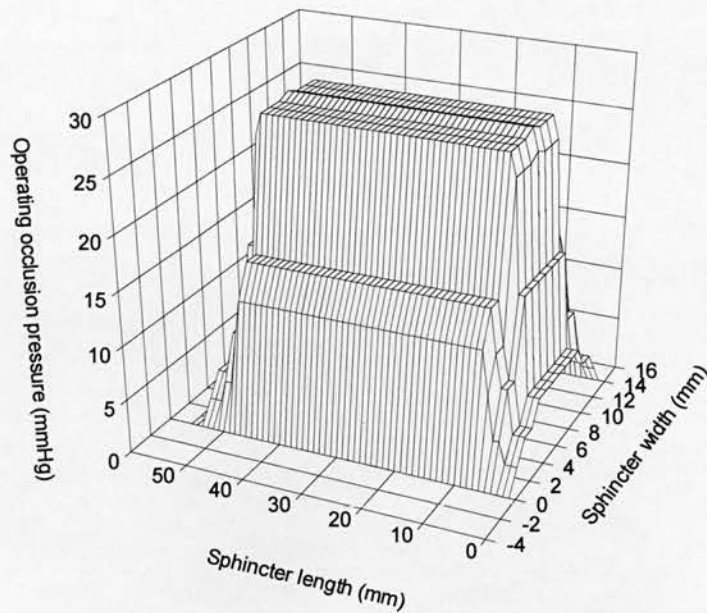


Figure 27: Pressure distribution on porcine bowel placed under the expander which was inflated to 40 mmHg. the straps were set at 22.5 mm separation as for the *in-vivo* experiments.

The pressure under the expander is distributed evenly without any localized high pressure points (Figure 27). Pressure transmission (operating occlusion pressure) on to the central portion of the bowel is approximately 60% of the internal expander hydraulic pressure.

There was no difference in the holdback pressure for water at bowel angulations of 90° and 180°. Figure 28 shows the holdback characteristics of the expander/pillow complex for semi-solid material. Holdback pressure enhancement is observed, especially at low sphincter pressures. Even when the sphincter is not inflated, a pressure of 36 mmHg has to be exerted before leakage is observed.

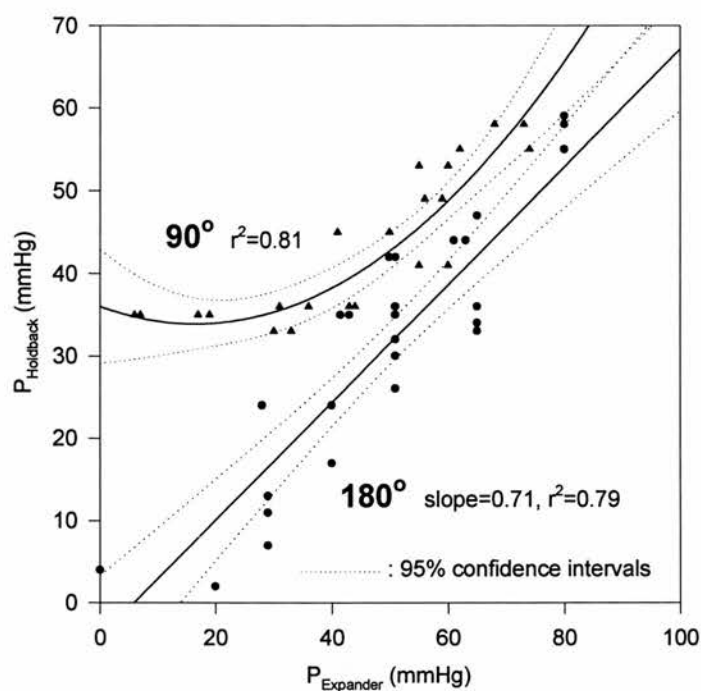


Figure 28: Holdback of semi-solid material *versus* expander inflation pressure for the AASP 2000.

The manually operated switch

In-vitro operation of the switch was satisfactory, and the presence of the thin silicone casing did not interfere significantly with tactile feedback and manipulation during activation and inactivation.

Study 2: In-vivo assessment

The pressure regulating balloon reservoir

The pressure *versus* volume curves of the balloons at implantation and at termination are plotted in Figure 29

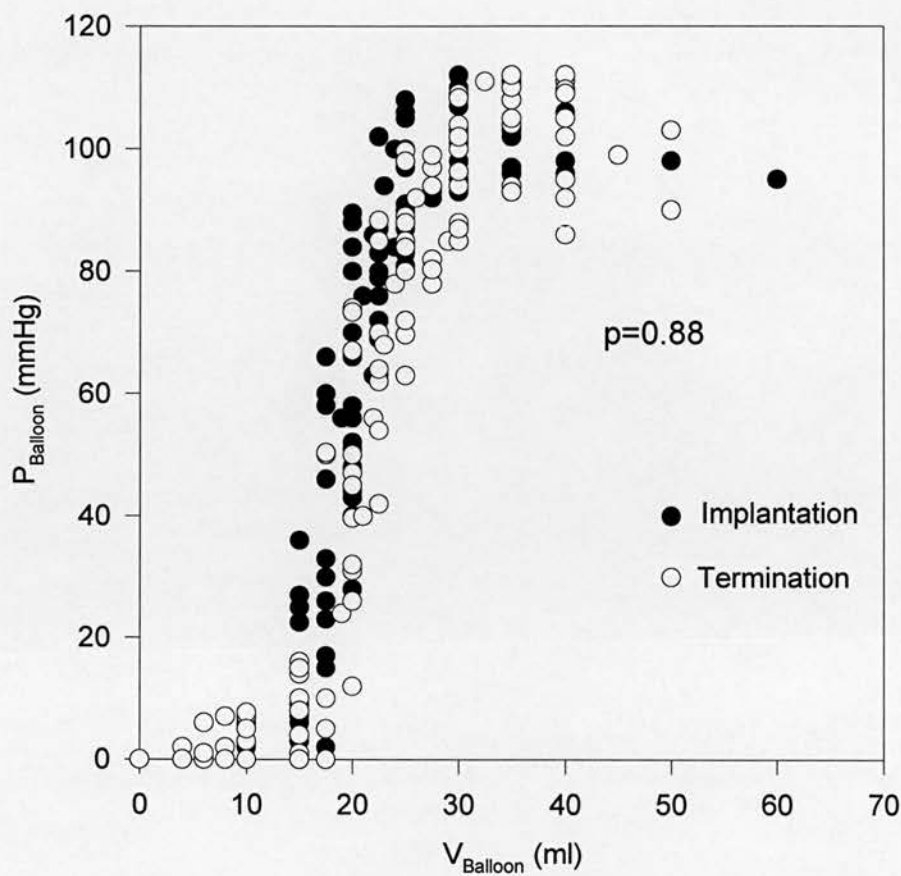


Figure 29: Comparison between the pressure *versus* volume curves of the balloons at implantation and at termination. The data from one encapsulated balloon are excluded.

The relationship is sigmoid as already demonstrated *in-vitro*. The rising slope of the sigmoid begins at a volume of approximately 15 ml and the plateau is achieved after 20-25 ml of inflation and maintained beyond inflation volumes of 50 ml. there

is no statistically significant difference between the pre- and post- implantation data ($p=0.88$).

In one animal the balloon became encapsulated due to the delayed onset of chronic prosthesis infection secondary to a bullous skin condition. The inflation characteristics of this balloon were analyzed separately and are shown in Figure 30. Upon inflation, the balloon pressure increased along a sigmoid curve as before, but at the expected plateau pressure and volume, the pressure continued to rise after only a short plateau. This was due to stretching of the capsule, which ruptured at a balloon volume of approximately 35 ml and pressure of 350 mmHg.

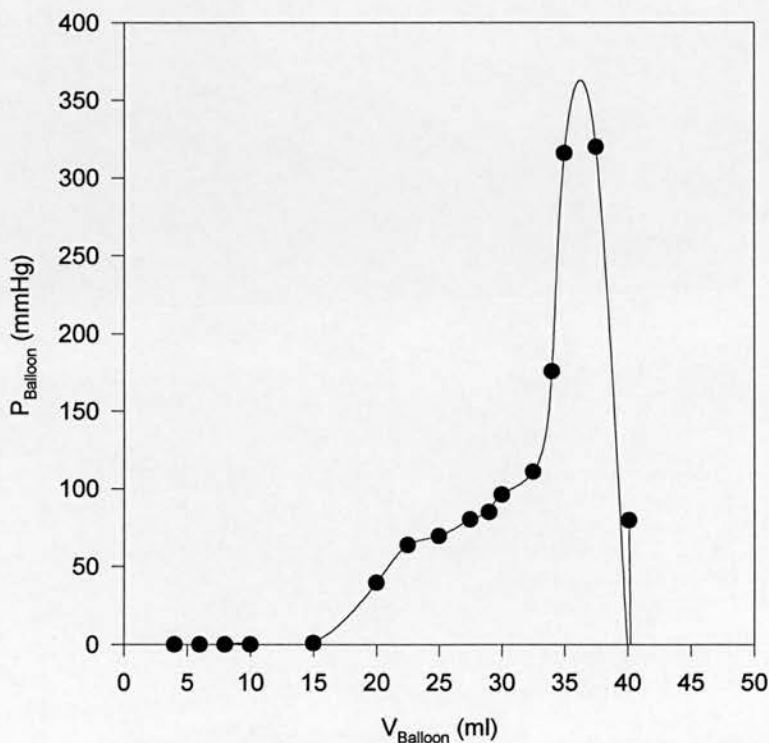


Figure 30: Pressure-volume relationship of the balloon which became encapsulated. The capsule becomes stretched after the balloon is inflated to 25 ml. The capsule ruptures at an inflation volume of 35 ml and balloon pressure of 350 mmHg.

The control pump

The operation of the control pump was unreliable and unsatisfactory. The problems encountered can be classified as relating to the shutoff valve, the resistor, the ball valves, the pump casing and injection port and the construction of the pump control channels and are summarized in Table 1.

The shutoff valve consisted of a simple piston type valve. This was easily displaced from its seat and caused inadvertent activation of the device leading to colonic obstruction. Sometimes the valve became partially displaced and acted as an unwanted one way mechanism that allowed flow from the balloon to the expander once again causing intestinal obstruction.

The narrow single lumen of the resistor had the tendency to get blocked due to corrosion (Figure 2) or debris left inside the casing during the manufacturing process. In one case, the resistor became dislodged from its place and caused intermittent obstruction by abutting onto the lateral wall of the pump casing.

In the ball valves there was a tendency to adhere onto the valve seat causing obstruction. They were made with polypropylene in the earliest version of the pump and it was initially thought that the adherence was due to electrostatic forces. They were subsequently replaced with ruby balls but the problem persisted. On close inspection through the pump casing under X2 magnification, it was demonstrated that the balls were being lodged into the valve seat during pumping. This caused distortion of the relatively soft silicone rubber which allowed the ball to become firmly embedded in the outlet channel causing subsequent obstruction to flow.

The pump casing stiffness was subjectively inconsistent. The bulb was too soft in at least two pumps which resulted in a decrease in suctioning efficiency. Fracture of the pump casing causing leakage of fluid occurred in one animal. Gradual fluid leakage necessitating replacement occurred on three occasions. Visible fluid leakage from the impalement sites of the injection port was observed in all explanted pumps.

The manufacturing of the pump allowed small particles of silicone to remain inside the voids and channels of the control mechanism casing. The presence of free particles tended to cause resistor blockage. The presence of irregularities, especially on the shutoff valve seat caused valve leakage.

The design of the casting of the control mechanism was also unsatisfactory. This allowed the presence of very narrow, angulated and tortuous channels inside the casing instead of direct fluid paths and caused impedance to flow. This was not the case for the AMS 800 valve, which had wide, short and straight fluid flow pathways (compare Figure 1 and Figure 2 with Figure 3 in Chapter 7).

Complication	Number of episodes	Animal IDs.
Shutoff valve malfunction	3, 18, 1, 7, 1, 4, 5, 11, 4, 15, 4, 2	2, 4, 5, 6, 7, 8, 12, 13, 15, 16, 19, 20
Resistor blocked		1, 13, 15, 19, 20
Resistor slow		7, 16
Resistor displaced		6
Ball valve malfunction		4, 6
Casing fracture		5
Bulb too soft		2, 15, 16, 19
Fluid paths too narrow		4, 7, 15

Table 1: Summary of pump complications.

The sphincter element

Figure 31 shows a plot of the sphincter internal hydraulic pressure *versus* the pressure measured at each inflation pressure by the pullthrough method (operating occlusion pressure). The slope of the regression line represents the proportion of transmission; this is approximately 60%.

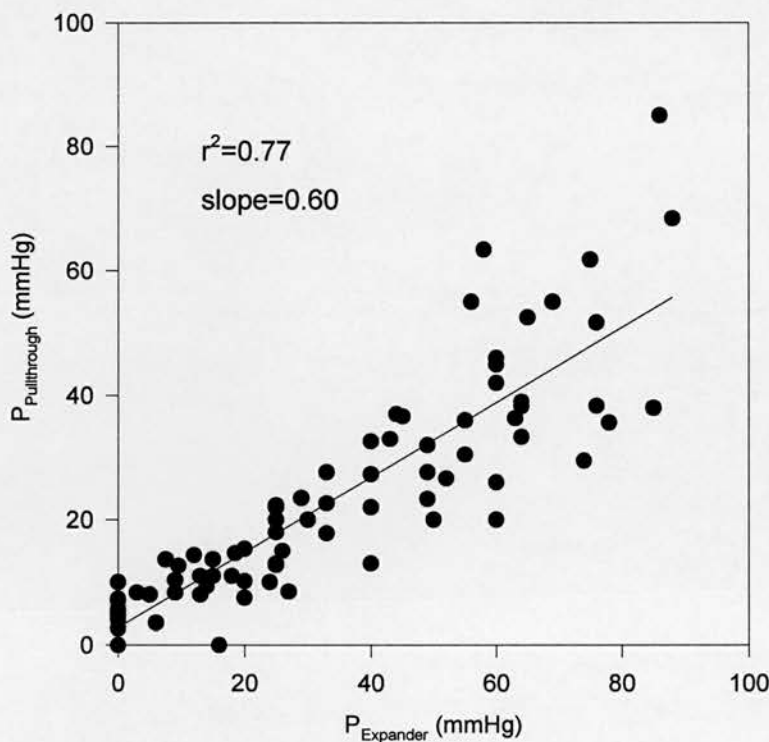


Figure 31: The proportion of pressure transmitted from the sphincter onto the bowel was 60%.

The pressure inside the sphincter increased more rapidly at similar inflation volumes at termination (Figure 32). This indicates that the compliance of the system decreased after implantation. This difference was statistically significant ($p<0.0001$).

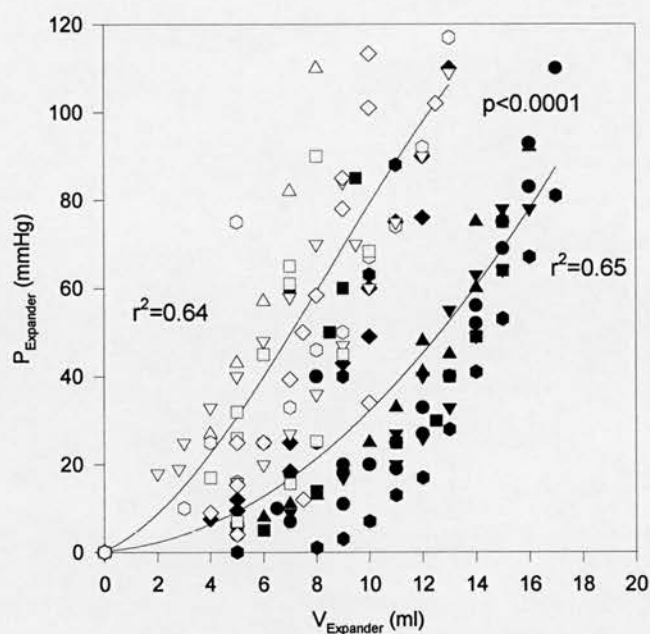


Figure 32: Plot of expander pressure-volume curves at implantation (solid symbols) and at termination (open symbols).

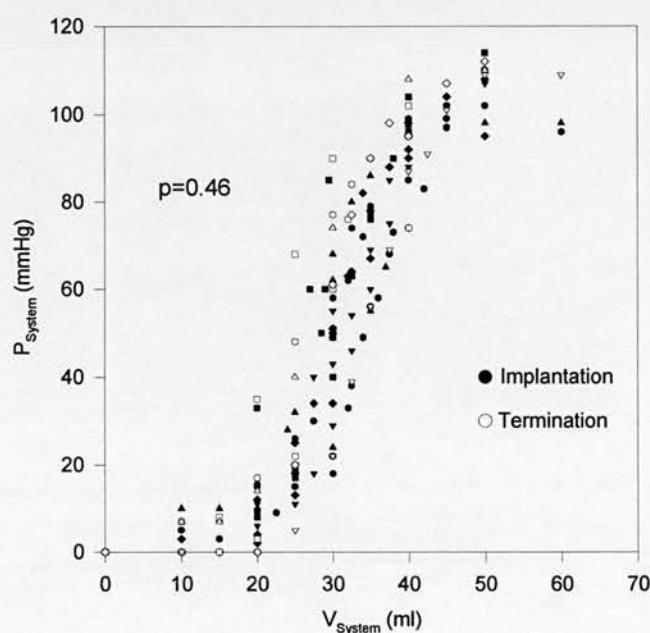


Figure 33: Plot of pressure-volume curves of the whole system (balloon, pump, expander *in-situ*) at implantation (solid symbols) and at termination (open symbols).

The pressure-volume relationship of the whole system at implantation and at termination is shown in Figure 33. There was no statistically significant difference between the data at implantation and at termination ($p=0.46$). The shape of the curves is sigmoidal and the plateau is at 100 mmHg. The rising slope of the sigmoid is at approximately 20 ml and the plateau begins at approximately 40 ml. These curves appear shifted to the right as compared to those of the balloon. There was no statistically significant difference between the pressure-volume relationship of the balloon and the whole system either pre- or post- implantation (Table 2).

P value	Balloon pre-implantation	Balloon post-implantation
Whole system pre-implantation	0.32	0.1
Whole system post-implantation	0.98	0.60

Table 2: Comparison between the non-encapsulated balloon and whole system pressure-volume relationships pre and post implantation.

The manually operated switch

Six animals had these devices implanted. The malfunction was discovered after activation was attempted for a control animal which had been deactivated for a prolonged period. This was due to the creation of vacuum inside the silicone casing of the switch when air was reabsorbed by diffusion due to a concentration gradient between it and the tissues. This created a force which collapsed the casing on to the switching element causing unwanted activation. Because of the collapsed casing, the switch could not be deactivated and became unusable (Figure 34). The pressure inside the casing was found to be -60 mmHg. Inadvertent activation occurred after as little as 9 days in one instance. Repeated measurements with time were made in two switches and the results appear in Figure 35. Use of this component was, therefore, abandoned and it was not developed further.

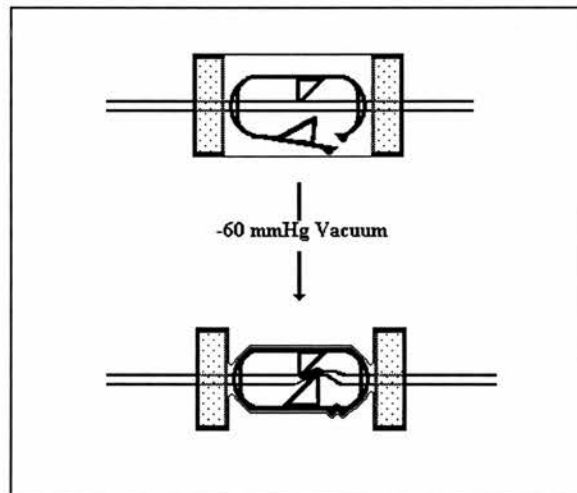


Figure 34: Unwanted activation of the hydraulic switch following absorption of air from the inside of the silicone casing. This creates a vacuum and collapses the casing onto the switch element.

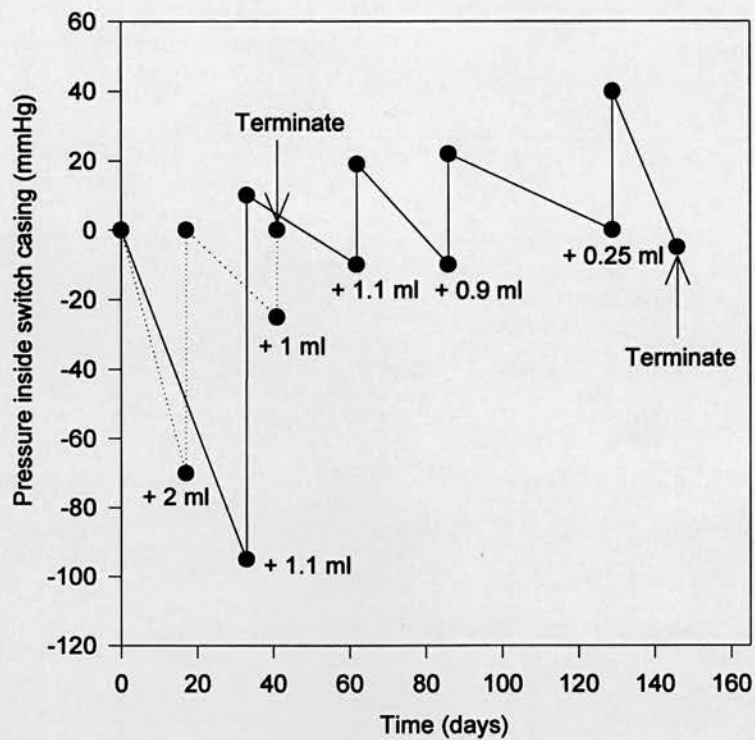


Figure 35: Plot of pressure changes inside the casing of two hydraulic switches with time.

Discussion

Two pressure regulating balloon prototypes were evaluated *in-vitro*: one manufactured by five and the other by six consecutive “dips” into molten silicone. The pressure-volume relationships of both consisted of sigmoidal curves reaching a prolonged plateau and showed hysteresis between the inflation and deflation phases. This is a well recognized property of silicone elastomers and it is utilized in artificial sphincter designs to provide pressure regulation below a chosen safe maximum level. The plateau pressure of the “5-dip” balloon was approximately 72 mmHg and this was thought to be appropriate for the animal experiments. As the amount of atrophy expected was not known in advance, it was decided to use the “6-dip” balloon (plateau = 100 mmHg) set at 60-70 mmHg operating pressure. This had the disadvantage of relying on a critical volume to maintain the operating pressure. It did, however, offer the possibility to increase the operating pressure to a higher level if required by injecting fluid into the system. Based on the survival animal data (Chapter 6) and the results of the blood flow experiments (Chapter 8), it is anticipated that the 72 mmHg balloon will be used in the preliminary human studies. This level is compatible with previously reported levels of pressure that can be safely applied onto the bowel in animals^{11,12} and humans⁹. The mechanical properties of the balloon did not change during the implantation period (Figure 29, Table 2) unless it became encapsulated (Figure 30). This occurred only in the presence of chronic infection. The balloon also maintained pressure regulation for the whole system during implantation (Figure 33), despite encapsulation of the expander with consequent decrease in the compliance of that component (Figure 32). The differences of the above data are normally distributed so it is reasonable to compare them with the t test. Even though non-parametric methods exist to assess the stochastic dominance of each curve and statistically compare them, the fact that the balloon and system sigmoid plots are visually overlapping and the unpaired t tests show no statistically significant differences strongly suggests that, if these tests were employed, the results would support the above conclusion.

The control pump used for these experiments was manufactured specifically for this study on a small scale using non-specialized tooling and materials. This fact has taken its toll on function and reliability both in the short and long term. The design of the casing of the control mechanism is outlined in Appendix 3. This allowed the presence of very narrow, angulated and tortuous channels inside the casing instead of direct fluid paths and caused impedance to flow. There was a significant pressure gradient across the fluid outlet pathway on the balloon side of the pump (>25 mmHg, Figure 12) which appeared to be due to the narrow and angulated fluid passageways as the pressure gradient across the ball valve is less than 2 mmHg. This was not the case for the AMS 800 valve, which had wide, short and straight fluid flow pathways (compare Figure 1 and Figure 2 with Figure 3 in Chapter 7). The ball valves were susceptible to “valve-lock” during operation. This was due to a soft valve seat which allowed the ball to become lodged inside it during the pumping action. A specially hardened valve seat is incorporated in the AMS device^{13,14} which did not suffer from this problem.

The shutoff valve consisted of a simple piston type arrangement as already discussed as opposed to its “waisted” barrel shaped counterpart in the AMS design. The valve travel of the AMS valve was also three times greater (Figure 2, Figure 3 in Chapter 7). These features offered increased reliability as indicated by the higher and more consistent unseating pressure of the AMS shutoff valve (Figure 9 - Figure 11). The fit of the shutoff valve inside its channel in the AASP 2000 must have been imperfect and allowed lateral movement which in many cases only allowed the valve to partially open. This created a one-way flow effect which caused partial obstruction sometimes in the direction of flow to the balloon and sometimes in the direction of flow towards the expander. The former caused colonic obstruction as the expander could not empty and the latter incontinence.

The presence of the fluid equilibrating resistor seemed to compromise pumping efficiency in both designs as it allowed some fluid to shunt into the expander during refilling of the pump bulb. The bulb of the AMS pump was made of stiffer material than that of the AASP which allowed it to create a greater suction and

have a faster bulb refill time. The diameter of this resistive channel is, therefore, critical. A single channel of 0.15-0.2 mm was used in the AASP design which produced an automatic re-occlusion time of approximately 5 minutes under ideal experimental conditions. This channel, however, had the tendency to block by debris left in the pump during the manufacturing process or stenose due to corrosion. AMS used a porous glass material^{13,14} of high composite connectivity (Appendix 1) which was much less susceptible to blockage by small particulate debris. This material, however, is susceptible to a different complication: if a gas bubble reaches the edge of the material, a high electrostatic field is created at the gas/fluid/solid interface¹⁵⁻¹⁷. This would denature any traces of proteinaceous material that might have been inadvertently introduced into the system fluid, cause crystallization of the contrast material at the interface and change the surface properties of the glass material. The above combination of effects would cause gradual deterioration, effectively causing stenosis and blockage of the resistor.

The advantage of having a resistor is that it provides automatic re-occlusion with no extra operations by the patient. This is especially useful in the control of micturition. Automatic re-occlusion, however, may not allow for complete bladder emptying in some cases if the 3-5 minute total re-occlusion time is less than the required voiding time. Even if the required voiding time was the same as the re-occlusion time, complete bladder emptying could still fail: when the sphincter is first deactivated urine will flow from the bladder to the outside across a high pressure gradient (Pressure gradient for urine flow = Bladder pressure - Sphincter pressure). Throughout the duration of micturition the bladder pressure will be decreasing and the sphincter hydraulic pressure increasing exponentially. Towards the end of micturition this pressure gradient will be severely reduced and, unless the bladder is completely emptied during the earlier part of the sphincter automatic re-occlusion period, a significant residual volume will remain inside it. Even an automatic re-occlusion time of 10 minutes would almost certainly not maintain the sphincter deactivated for long enough to allow bowel evacuation to be completed during evacuation, especially in the presence of semi-solid stool and bowel angulation

(Chapter 1). In addition, a higher re-occlusion time would require an effectively narrower resistor channel, which would have a greater chance of blockage. The AMS 800 pump characteristics, therefore, are not suitable to control an anal sphincter and the design of a new pump which circumvents these problems is being patented¹⁸ and will be discussed at the end of this thesis.

The device presented attempts to circumvent the problem of bowel ischaemia by introducing angulation of the bowel in order to decrease the pressure required to achieve continence (Chapter 1) and by applying this pressure in a gentle way to avoid the creation of localized high pressure points. By employing a linear expander gently flattening the bowel against a silicone filled pillow, a “hammock” effect is created on either side of the occluded bowel. This evenly distributes the occluding pressure (Figure 27) without the creation of single high pressure points (Chapter 4) and without “crenation” of the bowel which can be caused if a circular cuff was used⁹. The creation of the hammock effect is important as it is well established mathematically that if the contact surface between two pressurised chambers is distorted (e.g. folded sphincter cuff), the hammock effect disappears at the contact point. Under these conditions, all of the internal pressure of the system would be applied at that point (e.g. the apex of the cuff fold. See also Chapter 4). Holdback pressure enhancement by angulation of the bowel is obtained for semi-solid material, especially at low sphincter pressures (Figure 28). The results of this experiment are different to those for the circular cuff (Chapter 1: Figure 9), in that the holdback pressure does not increase exponentially with increasing inflation pressure. The latter effect is probably due to a combination of angulation and constriction introduced by the relatively narrow cuff (the lumen of the uninflated cuff had a radius of 11.9 mm, whereas the calculated flow through the AASP neosphincter would be equivalent to that through a circular orifice with 14.6 mm radius, see Appendix 1). Since resistance to flow is proportional to the fourth power of the radius of the conduit, the above parameters indicate that the resistance to flow would be 2.26 times greater through the circular cuff than the AASP 2000.

Extensive *in-vitro* studies were performed in order to determine the best geometry of the expander to ensure operation over a wide range of inflation volumes. This feature would be required to achieve the control of a sufficiently large lumen to allow the passage of bulky stool. The multiple compartment/concertina type of arrangement was employed to allow sufficient linear expansion for this to occur (Figure 3, Figure 19). The sphincter width was also chosen to closely resemble the length of the human anal canal high pressure zone¹⁹.

A series of mathematical manipulations were applied to indirectly calculate the compliance of the expander prototypes (Figure 20, Figure 21) based on their pressure-volume relationships. The calculated compliance is approximately 0.1 ml/mmHg for both expander prototypes but, as can be seen from Figure 21, the prototype with an increased cutout depth between the two elements of the concertina has allowed the device to remain useable with the same compliance over a greater range of inflation volumes (8→22 ml as opposed to 8→15 ml). An apparent paradoxical behaviour of the expander compliance at the limits of the operating inflation volume range is shown in this figure. This represents a flaw in the mathematical analysis which was plotted deliberately to discuss this point and should be ignored. The smooth part of the compliance curves corresponds to the range of volumes for which the pressure-volume data for each expander closely fit a third order polynomial regression. The paradox, therefore, occurs at the limits of this range and simply plots the inverse of the slopes of the polynomial equations and is of no relevance to the behaviour of the expander.

The pressure-volume characteristics of the expander were studied while it was attached to the pillow, at different levels of separation between the two. The separation was standardized by interposing specially constructed cylindrical sizers (diameter 20, 22.5 and 25 mm) between the expander and the pillow. The shape of the curves at 22.5 and 25 mm closely match that without the pillow (Figure 22, Figure 23) and in expander "B" the two are identical (Figure 23), indicating that the expander with a 3.5 mm cutout will operate under optimal conditions at a separation of 22.5 and 25 mm. At both these separations, a more acute contact angle was

achieved. This is a reflection of the difference of the shape of the apex of the expander at the moment it abuts onto the pillow at different degrees of separation. Creation of a contact angle is, therefore, another desirable feature of this device. The lumen created when the two components were separated by 20 mm was too small, whereas the whole system was too floppy at 25 mm and allowed displacement between the expander and the pillow to occur readily. A separation of 22.5 mm, therefore, appeared to be the best compromise and the two components were calibrated using the 22.5 mm sizer for all the *in-vivo* survival experiments. In mathematical terms, this was equivalent to fluid flow through a circular orifice of 29 mm diameter (Appendix 1).

Not all of the sphincter hydraulic pressure was transmitted onto the bowel wall, as part of it was dissipated to overcome the elastic properties of the expander: under the conditions described, approximately 60% of the expander internal hydraulic pressure was transmitted onto the bowel (Figure 31), which is similar to previously reported transmission factors for the circular cuff device (0.57²⁰, 0.6-0.8^{11,12}, 0.76²¹).

The risk of ischaemic complications would be expected to increase with increases of sphincteric occlusion pressure beyond a safe maximum; in fact, the number of revisions in a large series where the AMS circular cuff was assessed²² was proportional to the balloon pressure employed and increased once balloons of plateaus >70 cm H₂O (52 mmHg) were used. For all the above reasons, the setting of this pressure is one of the most critical factors of the preliminary assessment of the device.

Much of our knowledge on pressure tolerance of tissue placed beneath artificial sphincters come from the studies of Engelmann and his group^{11,12,23} on the AMS 800 device. This was implanted around intestinal loops in 22²³ and 40¹¹ New Zealand rabbits to evaluate its possible use for continent urinary diversion. This evaluation included the effects of varying closing pressures of the cuff on these isolated bowel loops. Sphincter-related complications (infection, erosion and

atrophy of bowel beneath the cuff) were pressure dependent and seen mainly in high pressure groups. In a canine model (n=24), balloon pressures of 70 to 80 cmH₂O were well tolerated by the bowel for up to 29 weeks with no evidence of erosion¹². The human sigmoid colon tolerates 70 cmH₂O (52 mmHg) whereas ischaemic erosion occurred at balloon pressures of 81-90 cmH₂O^{9,12} (60-66 mmHg). The actual pressure applied on the tissues is even lower as only part of the cuff pressure can be transmitted. This is of the order of 60% to 80%.^{11,12,20,21,24,25}. The novel design features of the AASP described above should allow it to be set at an operating occlusion pressure of approximately 40 mmHg (balloon pressure 70 mmHg, transmission factor 60%). The experimental results presented in this thesis suggest that this would be a safe choice in the minipig (Chapter 6) and humans (Chapter 8).

At present, the device is undergoing reliability testing by specially designed cycling equipment and also accelerated aging in a high temperature oven prior to a pilot study in human patients.

This artificial anal neosphincter appears to fulfill the required design criteria set at the beginning of the development process. The future development of the device would entail the design of a new and reliable control pump. Such a device, along with some other thoughts on the future development are presented at the end of this thesis.

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Section 2

Animal Implantation Experiments

Chapter 4

Preliminary studies and acute implantation

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Summary

The pressure distribution in the lumen of porcine bowel surrounded by a circular cuff was studied in an *in-vitro* model. The cuff occluded the lumen by the creation of a “triple cushion” effect. Directional variation of the pressure distribution inside the cuff lumen was demonstrated. In addition, the pressure was found to be disproportionately higher inside the cuff folds than in the center of the lumen. This could potentially cause crenation of bowel inside these folds and result in ischaemia.

The retention properties of such a cuff placed around the colon were studied for liquid, semi-solid and gas at different bowel angulations in a non-survival *in-vivo* porcine model. It was found that angle appeared to enhance the holdback of semi-solids but not of liquid or gas. Blood flow to the compressed colon was assessed by a Laser Doppler probe and was found to decrease at a higher rate than that of the increase in applied occlusion pressure.

The anatomical positioning of the AASP 2000 artificial Neosphincter was also assessed in preparation for the survival experiments.

Introduction

The results of the *in-vitro* experiments and theoretical analyses of fluid flow and holdback that were presented so far (Chapter 1, Appendix 1), indicate that the inclusion of angulation would allow an artificial anal sphincter to be set at a lower operating pressure yet still achieve continence of semi solids.

It has been reported¹ that the pressure distribution inside the lumen of the urethra surrounded by an inflatable cuff sphincter, shows no directional variability and such a sphincter has been used successfully for the control of urinary incontinence (see previous section). A modified urethral sphincter cuff has been implanted around bowel and has been assessed for the control of faecal incontinence in animal models²⁻⁴ and in humans⁵⁻⁹. The above results and also the results of the implantation of this device around bowel segments for other reasons⁹⁻²¹ indicate that bowel is less tolerant to circumferential pressure application than the urethra.

In this set of experiments, the effectiveness of a similar circular cuff sphincter was assessed *in-situ* in an acute non-survival porcine model. The pressure distribution inside the cuff lumen was plotted in order to compare it with previously reported experiments for the urethra¹. The effect of increasing occlusion pressure on colonic blood flow was also assessed by the Laser Doppler method.

Finally, the anatomical placement of the AASP 2000 Neosphincter prototype was studied in preparation for the survival animal experiments.

Materials and Methods

In-vitro and in-vivo measurements of intraluminal pressure and the effects of stool consistency and angulation:

Study 1a: In-vitro measurement of intraluminal pressure distribution in the circular cuff

Segments of porcine intestine were placed in a specially designed mechanical jig (see Chapter 1) and a circular sphincter (AMS cuff 75 mm circumference, 15 mm width) was placed around the bowel. A catheter tipped microtransducer (Gaeltec CTU1) was inserted into the lumen of the bowel proximal to the cuff through a small incision and fixed in place by a purse-string suture. The device was inflated by injecting water and the cuff pressure (P_{Cuff}) measured by a solid state pressure transducer (Baxter Uniflow, model DPT). Upon inflation, the bowel lumen was occluded by the creation of a “triple cushion” effect (Figure 1). Another catheter tipped microtransducer was then placed in the center of the cuff lumen and rotated by 360° while the pressure was continuously recorded (Figure 2).

Water was infused into the bowel at a rate of 1 ml/min and the pressure at which leakage was observed through the sphincter was noted (P_{Leak}). At each inflation pressure, a catheter tipped microtransducer was placed inside the cuff fold and the pressure measured (P_{Angle}).

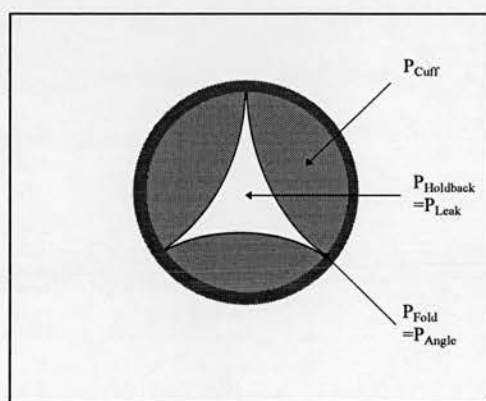


Figure 1: Occlusion of the bowel lumen by a circular cuff. Upon inflation, a “triple cushion” effect is created which compresses the bowel to close the lumen.

Study 1b: In-vivo assessment of the circular cuff sphincter

A circular cuff sphincter (width 22 mm) has been tested in a study of 6 female minipigs. Each animal was given a premedication dose of Atropine Sulphate 0.04 mg/kg and Azaperone (Crow Chemical Co. Ltd) 0.2 ml/kg intramuscularly. Anaesthesia was induced and maintained with Halothane (5% and 1-2% respectively) via an endotracheal tube. The peritoneal cavity was approached via a mid-line incision and the rectum was mobilized. The circular cuff was placed snug around the lower rectum through a mesenteric window.

The cuff was then inflated with water and the pressure inside it measured with a pressure transducer (Baxter Uniflow model DPT). At each inflation pressure, the intraluminal bowel pressure was measured by a catheter tipped transducer (Type CTU1 Gaeltec Ltd, Isle of Skye) using the station pullthrough technique. The active surface of the transducer was orientated onto the dome of the cuff cushion.

The bowel proximal to the cuff was then filled with either air, saline or semi-solid material (faeces, toothpaste or a mixture of oatmeal, KY jelly and calamine lotion in water to achieve a paste of "soft" or "hard" consistency - see Appendix 4). Pressure was applied manually on to the proximal bowel until the gas, liquid or solid just leaked through the cuff sphincter. The pressure at which leakage occurred was measured by a catheter tipped microtransducer secured inside the lumen of the proximal bowel by a purse-string suture. This procedure was performed at no bowel angulation (180°) and repeated at various degrees of angulation of the bowel at the site of the cuff (90°, 135°).

Study 2: Measurement of blood flow

The working principle of Laser Doppler flowmetry has previously been described in detail²²⁻²⁵. In this study we used the PeriFlux PF2 Helium-Neon Laser unit (Perimed Ltd, Sweden) with the following characteristics: wavelength 632.8 nm,

probe light output 1 mW, fiber diameter/separation 0.7/0.7 mm (one emitting and two receiving fibers), measurement radius 1 mm, frequency shift limit 12 KHz, gain setting $\times 10$, time constant 3 s. A specially made flanged probe was used which rested on the bowel with minimal application of pressure.

Six adult female pigs were used. The probe was placed on the colon just distal to the expander avoiding the tænia coli and a reading was taken once steady state conditions were reached as determined by the presence of a pulsatile flow signal and a steady reflected signal. The colon distal to the sphincter was divided in four animals and left *in-situ* in the other two. The measurements were repeated with progressive inflation of the cuff. At each cuff inflation pressure, the operating occlusion pressure on the bowel was determined by measuring the intraluminal pressure by a catheter tipped microtransducer (Gaeltec, CTU1) using the station pullthrough technique. Blood flow values were given in relative perfusion units ($V \times 10$) and these were correlated with the measured operating occlusion pressure.

Study 3: Anatomical positioning of the AASP 2000 prototypes

Five adult female animals were used in this preliminary study. Under halothane anaesthesia, an infra-umbilical midline laparotomy was performed. The small bowel and uterine horns were retracted and the descending colon/rectum delivered into the wound. The AASP 2000 prototype was placed as low in the pelvis as possible. In two animals the placement of the expander or pillow through a window of the colonic mesentery was studied. In another animal, rehearsal implantation of the whole system was performed. In the last two animals, the whole system was implanted and its operation was assessed as follows: the expander was passed through a small window in the rectal mesentery and the pillow attached anteriorly by the securing straps. The expander was progressively inflated with water in a stepwise manner and the system pressure measured by a solid state transducer (Baxter Uniflow model DPT). The operating occlusion pressure was measured by the station pullthrough technique as above. The bowel was then transected

approximately 5 cm distal to the Neosphincter and a catheter tipped microtransducer was placed into the lumen proximal to the sphincter through a small incision and secured with a purse-string suture. The proximal bowel was filled with either saline or toothpaste and the sphincter activated. Pressure was applied manually on to the proximal bowel until the liquid or solid just leaked through the Neosphincter. The pressure at which leakage occurred was measured by the catheter tipped microtransducer as above.

Results

The vital statistics of the animals are summarized in Table 1.

		S.D.
BP (sys/diast, mmHg)	82/51	6.7/5.4
Bowel width (mm)	38.7	4.8
Bowel thickness (mm)	1.45	0.5

Table 1: Vital-statistics of animals used in the acute experiments.

Study 1a:

The pressure distribution inside the cuff lumen was heterogeneous (Figure 2): it varied according to the angular orientation of the microtransducer and the peaks corresponded to the domes of the cuff cushions (Figure 1). The leakage pressure was approximately 49% of the cuff pressure (transmission factor = 0.49, Figure 3). The transmission factor inside the angle between the cuff cushions increased rapidly with inflation of the cuff to almost 1.00 (transmission 100%).

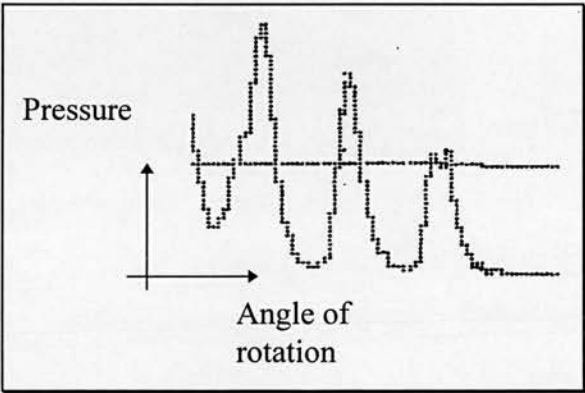


Figure 2: Pressure inside the lumen of bowel surrounded by a circular cuff sphincter as a function of angular orientation of the pressure measuring transducer. Peaks of pressure correspond to the sites of the cuff cushion domes.

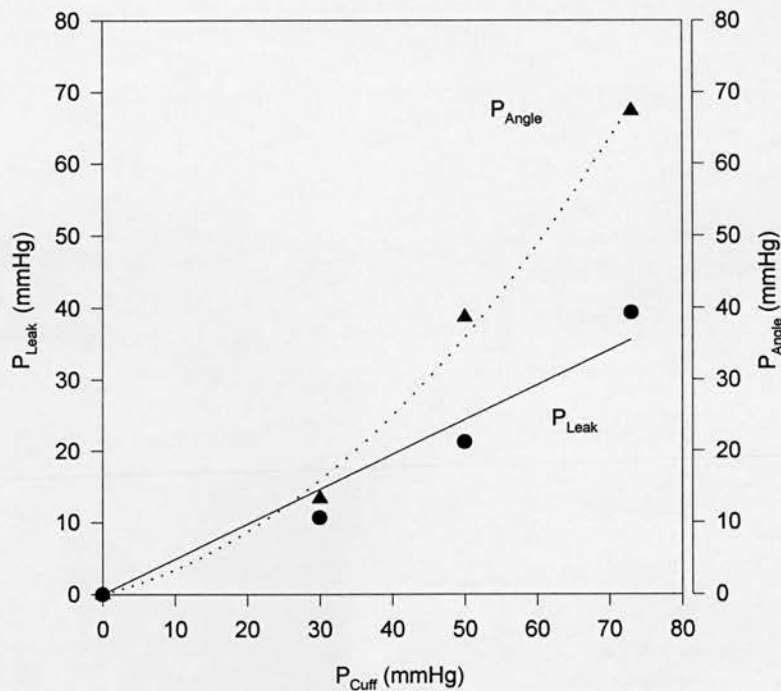


Figure 3: Plot of cuff inflation pressure versus holdback pressure for liquid (P_{Leak}) or pressure inside the angle between the cuff cushions (P_{Angle}) of circular sphincter.

Study 1b:

Approximately 80% of the cuff pressure was transmitted onto the bowel wall at the sites of the cuff cushion domes (transmission factor = 0.79, represented by the slope of the regression line in Figure 4).

The transmission factor for holdback of liquid at 180°, i.e. no bowel angulation (Figure 5) was virtually the same in the *in-vitro* and *in-vivo* studies (0.49 and 0.47 respectively). There was no difference in the holdback characteristics of bowel at 180°, 135° or 90° (Figure 6, Table 2).

The transmission factor for holdback of gas was <0.20 in all animals and at all angulations with no statistically significant difference between the presence or absence of angulation ($p=0.35$).

As the semi-solid substance used in the experiments was not standardised, meaningful comparison between the different animals is not possible. The following generalization can, however, be made: for all semi-solids tested, leakage occurred at a higher intraluminal pressure for any given cuff inflation pressure and the presence of bowel angulation appears to enhance this phenomenon even further.

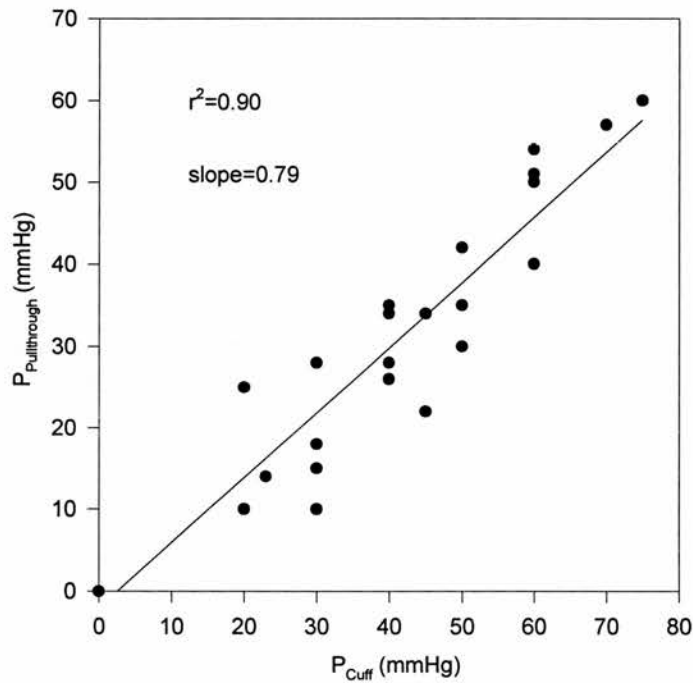


Figure 4: Operating occlusion pressure ($P_{Pullthrough}$) in porcine bowel as a measure of circular cuff pressure (P_{Cuff}).

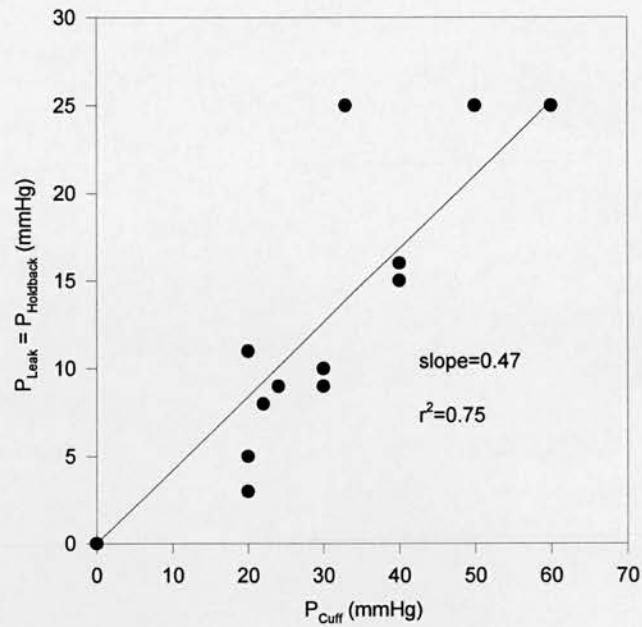


Figure 5: Plot of cuff inflation pressure versus holdback pressure of circular sphincter for liquid (P_{Leak}) without bowel angulation.

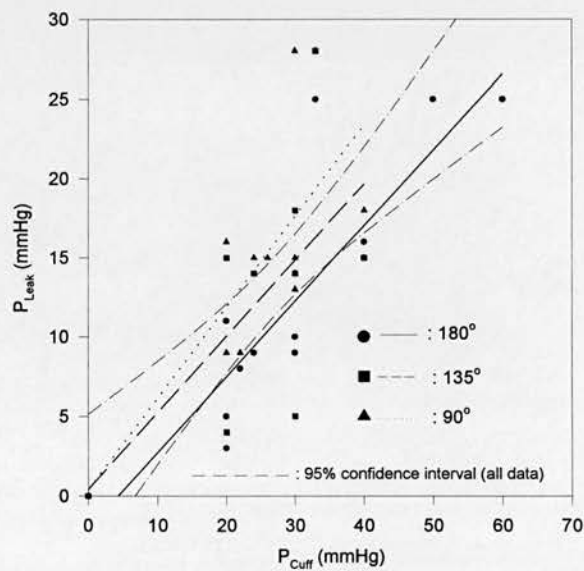


Figure 6: Plot of cuff inflation pressure versus holdback pressure of circular sphincter for liquid (P_{Leak}) at no bowel angulation (180°) and angulations of 135° and 90°.

Bowel Angulation	Transmission factor	r^2
180°	0.47*	0.75
135°	0.48	0.42
90°	0.57*	0.55
All data	0.47	0.53

Table 2: Transmission factors for holdback of liquid in bowel by circular cuff sphincter. *: $p=0.22$.

Study 2:

The baseline blood flow was 111.2 (S.D.=51.5) relative perfusion units (RPU's). As the baseline blood flow range was wide (Figure 7), the standardised value (% of baseline) was used for analysis of blood flow *versus* cuff inflation pressure (Figure 8).

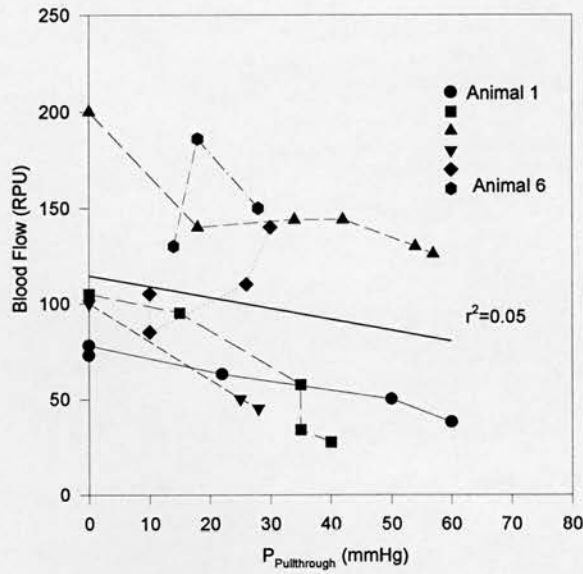


Figure 7: Blood flow in the six animals studied *versus* increasing cuff inflation pressure.

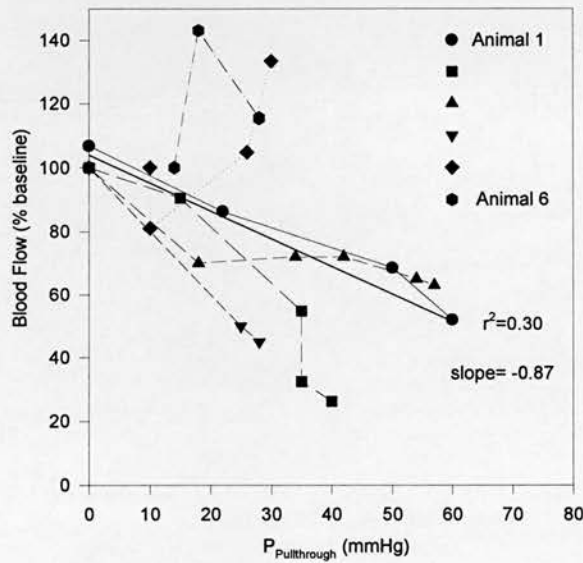


Figure 8: Blood flow in the six animals as a percentage of baseline flow *versus* increasing cuff inflation pressure.

Blood flow decreased with increasing cuff inflation pressure in four animals, but showed a paradoxical increase in another two ($r^2=0.30$, slope= -0.87 shown in Figure 8). In these two animals, the distal colon was not divided. If these two animals are excluded from the analysis, the correlation becomes stronger without affecting the slope of the regression line which represents the rate of decrease of blood flow at increasing cuff inflation pressure ($r^2=0.51$, slope=-0.84 shown in Figure 9). Overall, when the cuff inflation pressure was increased, the blood flow decreased at almost the same rate (-0.84) as the rate of increase in the operating occlusion pressure (0.79, Figure 4).

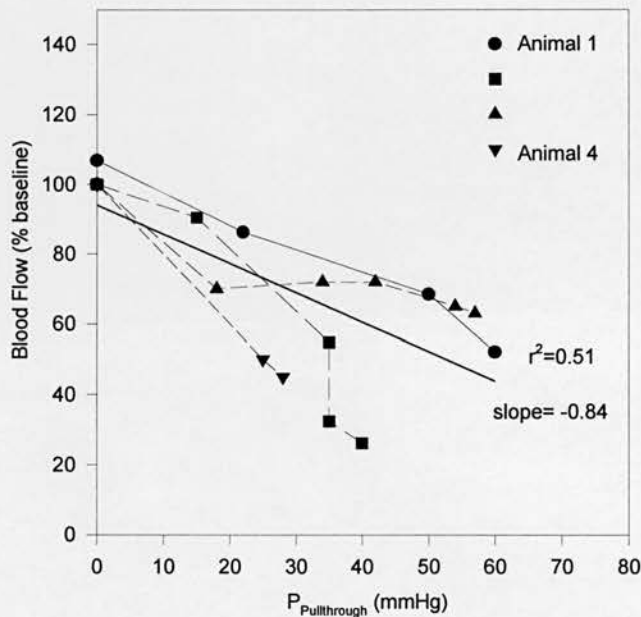


Figure 9: Blood flow as a percentage of baseline flow in the four animals in which paradoxical increase was not observed *versus* increasing cuff inflation pressure.

Study 3:

Once the anatomical placement of the device was established in the first three minipigs, the holdback pressure characteristics of the AASP 2000 prototype were studied without bowel angulation in a further two animals by using the same methodology as that in Study 1b above.

The expander pressure transmission factor for liquid was virtually identical when studied by the station pullthrough method or by measuring the holdback pressure (0.48 and 0.45 respectively, Figure 10). Holdback pressure was also slightly greater for semi-solid material (toothpaste).

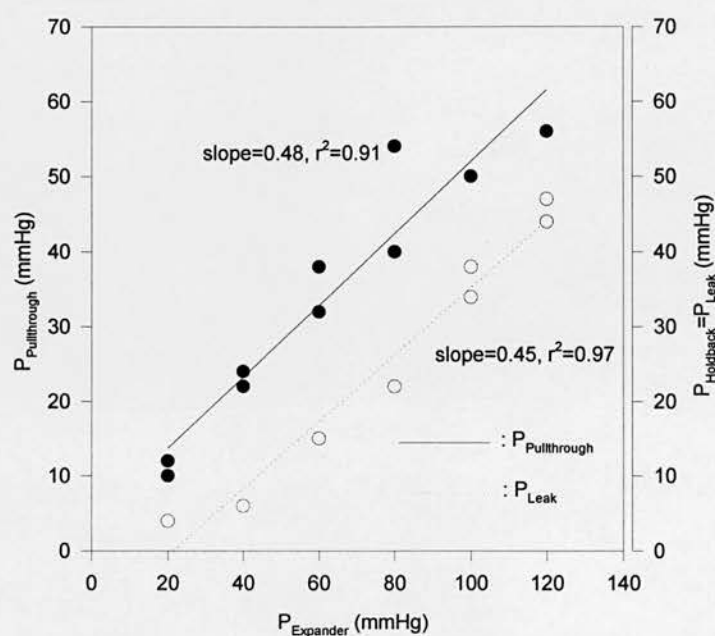


Figure 10: Fluid retention characteristics of bowel with Neosphincter prototype.

Discussion

In this set of experiments, the disadvantages of the circular cuff sphincter have been demonstrated. The pressure distribution inside the cuff lumen is not even: localized areas of high pressure exist at the domes of the cuff cushions and also inside the cuff folds. It has been reported¹ that the pressure distribution inside the lumen of the urethra surrounded by an inflatable cuff sphincter, shows no directional variability. This was not shown to be the case for bowel in this study. This may be due to the fact that variations of external pressure can be measured more readily through the thinner bowel wall, but it is more likely that the relatively crude perfusion catheter used by Blok and his co-workers¹ was neither sensitive nor selective enough to detect the changes in pressure distribution. The risk of ischaemia may be increased as the triangular lumen of the circular cuff may cause crenation of the thin wall of the bowel into the high pressure zones of the cuff folds¹⁶. It is well established from engineering analysis of the "hammock effect", which is created when two compliant pressurized surfaces abut on one another, that if a point of disruption of the smooth contour of an inflatable element exists (e.g. the apex of the cuff fold in this case) the pressure inside this element is reflected into the lumen²⁶. This was confirmed in this study by the fact that pressure transmission inside the cuff fold approached 100%.

As it is well demonstrated that the bowel is not tolerant to the application of excessive circumferential occlusion pressure^{2-4,9-21}, the even distribution of intraluminal pressure afforded by the AASP 2000 Neosphincter represents a definite design advantage.

A sphincteric effect based on the creation of the "triple cushion" effect has another disadvantage when used to occlude the bowel lumen. As the thin bowel wall cannot buffer a heterogeneous pressure distribution, low pressure zones are interposed between high pressure areas and this, combined with the poor fluid sealing properties of the bowel mucosal surface, increases the chance of fluid leakage through these low pressure paths. This is reflected by the fact that the operating

occlusion pressure measured at the cuff cushion domes is much greater than the holdback pressure for liquid at the same cuff inflation pressure (transmission factors of 0.79 and 0.47 respectively). The AASP 2000 does not appear to suffer from this disadvantage because the pressure distribution inside its lumen is even (Chapter 3) and the transmission factors for the operating occlusion pressure and holdback pressure *versus* expander pressure are almost identical (0.48 and 0.45 respectively). Another advantage of this design is that the transmission factor can be set to a required level by adjusting the slack of the securing straps of the expander (see Chapter 3, Chapter 6 and Appendix 3).

The effect of angulation was as expected and followed the principles demonstrated in Chapter 1. There was no difference in the retention properties for air or water between angled and straight bowel, whereas angulation seemed to enhance the retention of semi-solids. No quantitative comparisons for semi-solid holdback can be made due to the heterogeneity of the substances tried (Appendix 4). For this reason, a standard gel simulating faeces was designed (Appendix 2) and evaluated (Chapter 1).

The blood flow in the colon was measured by Laser Doppler flowmetry. The working principle of this method has previously been described in detail²²⁻²⁵. The technique has been used to assess gastrointestinal blood flow in animals²⁷⁻³⁴ and humans^{33,35-43} and was shown to have a measuring depth of 6 mm in human colon^{44,45}, i.e. transmural measurements are obtained. A review of this technique and its evolution will appear in Chapter 8. The equipment available has the disadvantage of measuring blood flow in a very small volume of tissue and in addition it is very sensitive to movement artefacts, hence the wide variation of baseline blood flow reading. A new method of blood flow measurement which does not have the disadvantages of the static Laser single point method used here will be described in Chapter 8.

For the above reasons, the blood flow decrease was standardised for all animals by measuring the percentage compared to the baseline flow value for each

occlusion pressure. When the cuff inflation pressure was increased, the blood flow decreased at almost the same rate as the rate of increase in the operating occlusion pressure (-0.84 % per mmHg occlusion pressure and 0.79 mmHg occlusion pressure per mmHg cuff inflation pressure respectively). It has been shown in this study, however, that the operating occlusion pressure is not a true representation of the efficacy of retention of liquid by a circular cuff sphincter. In this case, the relevant transmission factor is 0.47 mmHg holdback pressure per mmHg cuff inflation pressure. This means that when a circular cuff is used as a sphincter around bowel, it causes a disproportionately higher decrease in blood flow for a modest increase in holdback pressure.

Following the above discussion and the design analysis of the AASP 2000 outlined so far, it seems that this device has definite advantages over a circular cuff sphincter and its assessment in survival animal experiments and in human volunteers will be described in the subsequent chapters of this thesis.

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Chapter 5

Bowel transit studies

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Summary

In this experiment, the bowel transit time of the Yucatan minipig was studied in three of our experimental animals using the radioopaque marker and chromic oxide ingestion methods. Both methods had drawbacks and these are discussed. The latter was less disruptive, but was only suitable to determine the mouth to anus time. The mouth to anus time was less than 24 hours. Within the limitations of small number of animals in the radioopaque marker study, the mean colonic transit time was found to be of the order of 28 hours; the presence of the deactivated neosphincter did not appear to influence the transit time.

Introduction

Measuring colonic transit time can be of value in the investigation of patients with slow transit constipation. Transit can be measured by ingesting a number of radioopaque markers and obtaining an abdominal X-ray every day to count the number and distribution of the remaining markers in the colon¹. Segmental and total colonic transit time can thus be estimated. This was found to be variable^{1,2}, but it has been reported that in normal people most of the markers (80%) should be expelled by the fifth day¹.

The transit time was studied in the experimental animals in order to establish its length and also to determine whether it is affected by the presence of the neosphincter. It was not possible to X-ray the animals daily, as a general anaesthetic or heavy sedation was required each time an X-ray was taken. A simplified method was, therefore, attempted whereby three different markers were administered one on each day, and an X-ray taken on the fourth day³. The mouth to anus time was also assessed using the chromic oxide ingestion/excretion method⁴.

Materials and Methods

The radiological and chromic oxide studies were performed simultaneously in order to minimize intra-animal variations and also avoid the potential interference of the administration of a general anaesthetic to the transit time.

Radioopaque marker study³

Three kinds of radioopaque markers were used: lead shot, nylon rings and Teflon rods measuring approximately two to four millimeters. The study animal received 20 markers each day mixed with food. One kind was given on each day. The animal was then anaesthetised on the fourth day (technique described in Chapter 6) and a plain X-ray of the abdomen obtained (Figure 1, Figure 2). The number of remaining markers were counted and the mean colonic transit time (MCT) was calculated by the formula³:

$$\text{MCT} = 1.2 \times (N_1 + N_2 + N_3)$$

Where N_{1-3} are the numbers of each type of marker remaining in the abdomen.

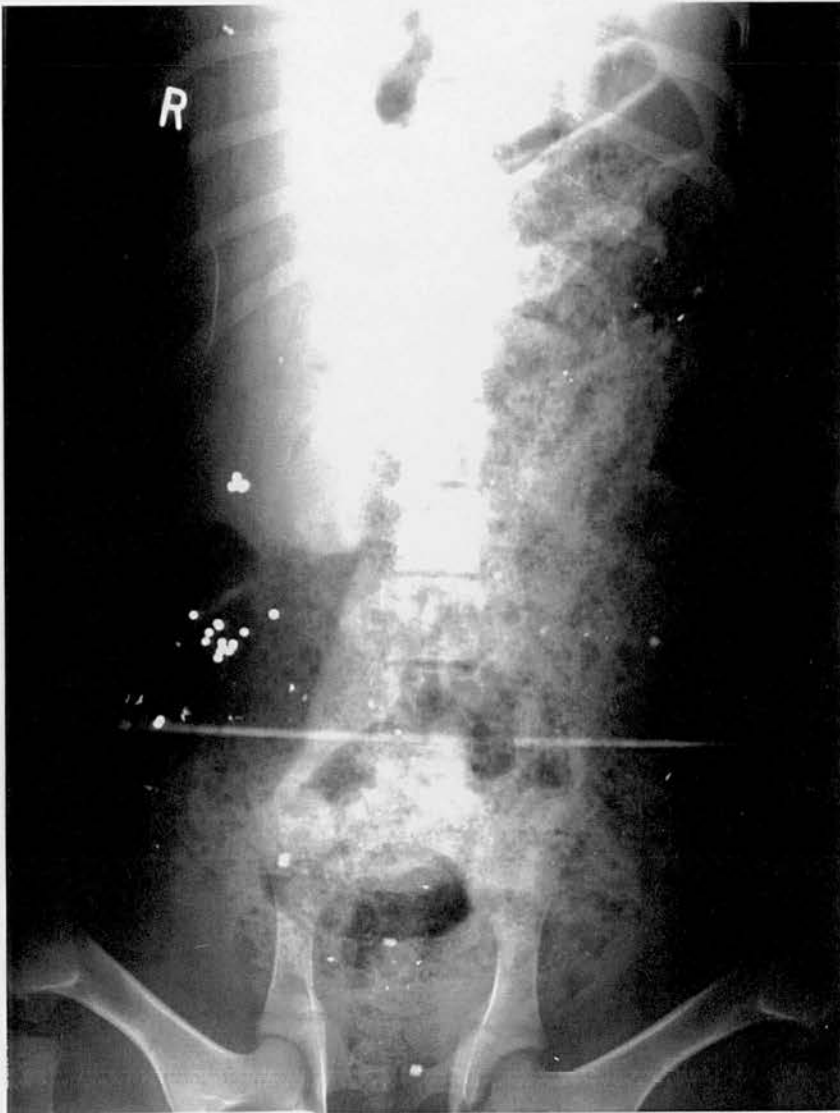


Figure 1: Radioopaque marker study in non-operated animal. Twenty markers were given on each day for three days. X-ray taken on fourth day.

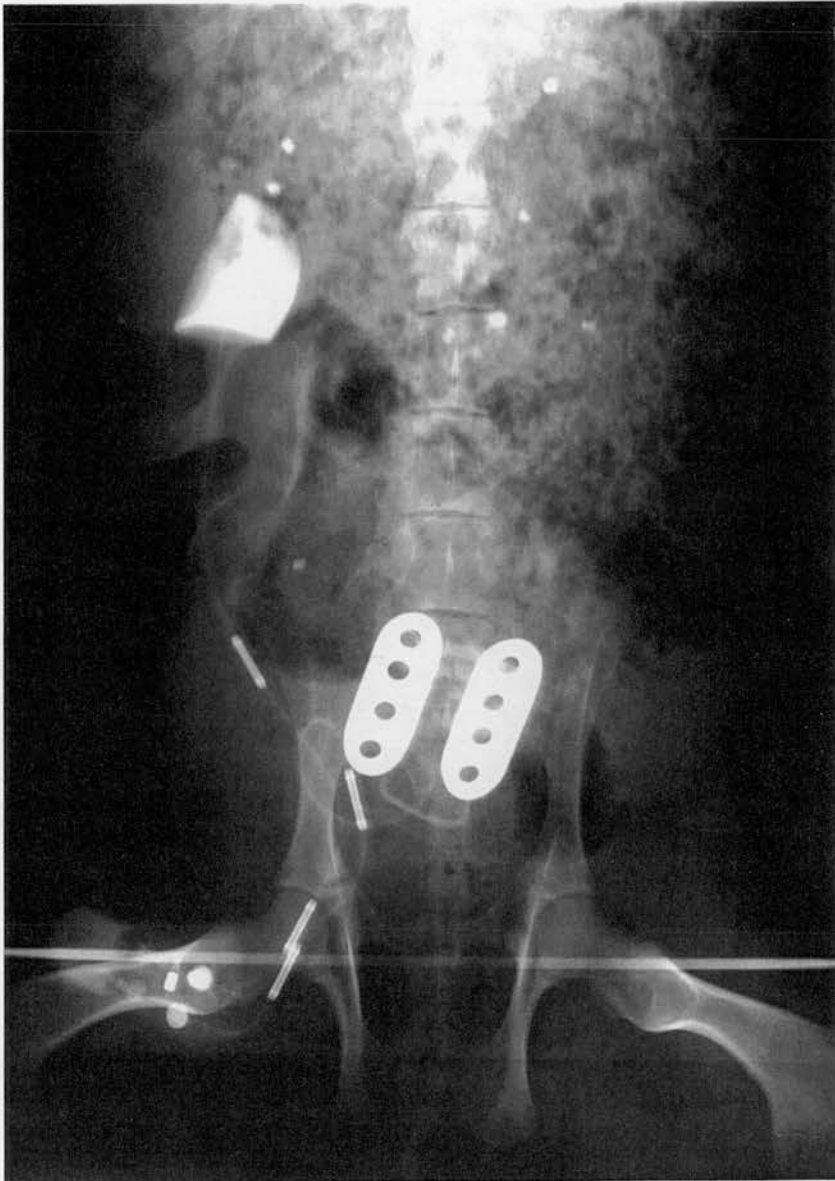


Figure 2: Radioopaque marker study in animal with deactivated prosthesis.

The study was performed twice on three animals. One of the animals had no operation, the second had a deactivated device in-situ and the third animal was studied on separate occasions when the sphincter was activated and deactivated.

Chromic oxide ingestion study⁴

1 or 10 grams of chromic oxide were mixed with a small amount of wet diet and then added to the morning feed. 50 grams of fresh faeces were collected approximately every two hours following feeding of the marker powder until 17:00 and again the next day. Gloves and masks were worn whenever the chromium powder or faeces were handled.

The following reagents were prepared and used for the analysis:

- Phosphoric Acid - Manganese Sulphate Solution:
30 ml 10% w/v $\text{MnSO}_4 \cdot 4\text{H}_2\text{O}$ solution in 1 liter 85% H_3PO_4
- Potassium Bromate Solution:
4.5% w/v
- Calcium Chloride Solution:
109.32g $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$ made up to 1 liter
- Stock Silicate Solution:
2.78g $\text{Na}_2\text{SiO}_3 \cdot 5\text{H}_2\text{O}$ made up to 1 liter
- Stock Chromium Solution:
2.8285g $\text{K}_2\text{Cr}_2\text{O}_7$ made up to 1 liter (1 mg/ml)

The faeces were prepared for analysis as follows: a faecal sample was dehydrated and ground. 0.5g of dried ground sample was ashed at 600° for 1½ hours and then cooled. 1.5 ml H_3PO_4 - MnSO_4 solution and 2 ml KBrO_3 was then added, the sample covered with a watch glass and digested on sandbath until effervescence stopped and a purple colour appeared. The solution was cooled and filtered and made up to 100 ml in a volumetric flask containing 2.5 ml CaCl_2 and 5 ml Silicate solutions.

An Atomic Absorption Spectrophotometer, Perkin Elmer 2380, (Perkin Elmer Ltd., Post Office Lane, Beaconsfield, Bucks, HP9 1QA) was used to measure the absorption of chromium at a wavelength of 340 nm. An absorption curve was drawn

from the absorption of standard solutions. Each standard solution contained the following:

- 3 ml $\text{H}_3\text{PO}_4 \cdot \text{MnSO}_4$ solution
- 4 ml KBrO_3 solution
- 5 ml CaCl_2 solution
- 10 ml Na_2SiO_3 solution and
- 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 or 4.0 ml of Chromium solution.

Each mixture was then made up to a total volume of 200 ml. The resulting standard solutions contained Chromium at concentrations of:

0, 2.5, 5.0, 7.5, 10.0, 12.5, 15.0 and 20.0 $\mu\text{g/ml}$.

The Atomic Absorption was read at 340 nm and the chromium concentration determined from the graph made from the above standard solutions.

Calculation:

Let X = reading in $\mu\text{g/ml}$:

$$X(\mu\text{g} / \text{ml}) \times \frac{100\text{ml}(\text{total volume})}{1000(\mu\text{g} / \text{mg})} \times \frac{1000(\text{g} / \text{kg})}{1000(\text{mg} / \text{g})} \times \frac{1}{\text{weight}(\text{g})} \therefore$$

then the concentration of chromium $[\text{Cr}]$ in the sample in g/kg (or ‰ w/w) of sample would be:

$$\boxed{[\text{Cr}] = \frac{X \times 0.1}{\text{weight}} \text{ g / kg}}$$

The study was performed on the same three animals. Two had no operation and the third had a deactivated device *in-situ*. The study was performed four times in the first animal (twice using 1g and twice using 10g of chromic oxide), twice in the second animal (using 1g of chromic oxide) and once in the third (using 10g of chromic oxide). The experimental animal details are summarized in Table 1.

Animal ID	Chromic Oxide 1g	Chromic Oxide 10g	Marker Study
#16		deactivated	deactivated
#16			activated
#19	no-operation		deactivated
#19	no-operation		deactivated
#20	no-operation	no-operation	no-operation
#20	no-operation	no-operation	no-operation

Table 1: Summary of the experimental animal details.

Results

Radioopaque marker study

The results of this study are summarized in Table 2. It appears that activation of the sphincter prolongs the transit time, but its mere presence does not. Statistical analysis is not possible due to the small number of animals. Counting of the markers was not possible on one occasion because the animal chewed the markers (Figure 3).

Animal ID	Type of animal	Number of markers left	Transit time (hours)
#16	deactivated	24	28.8
#16	activated	36	43.2
#19	deactivated	*	*
#19	deactivated	12	13.6
#20	no-operation	18	21.6
#20	no-operation	30	36

Table 2: Summary of the results of radioopaque marker transit study. In one instance (*) the estimation was impossible as the animal chewed the markers.

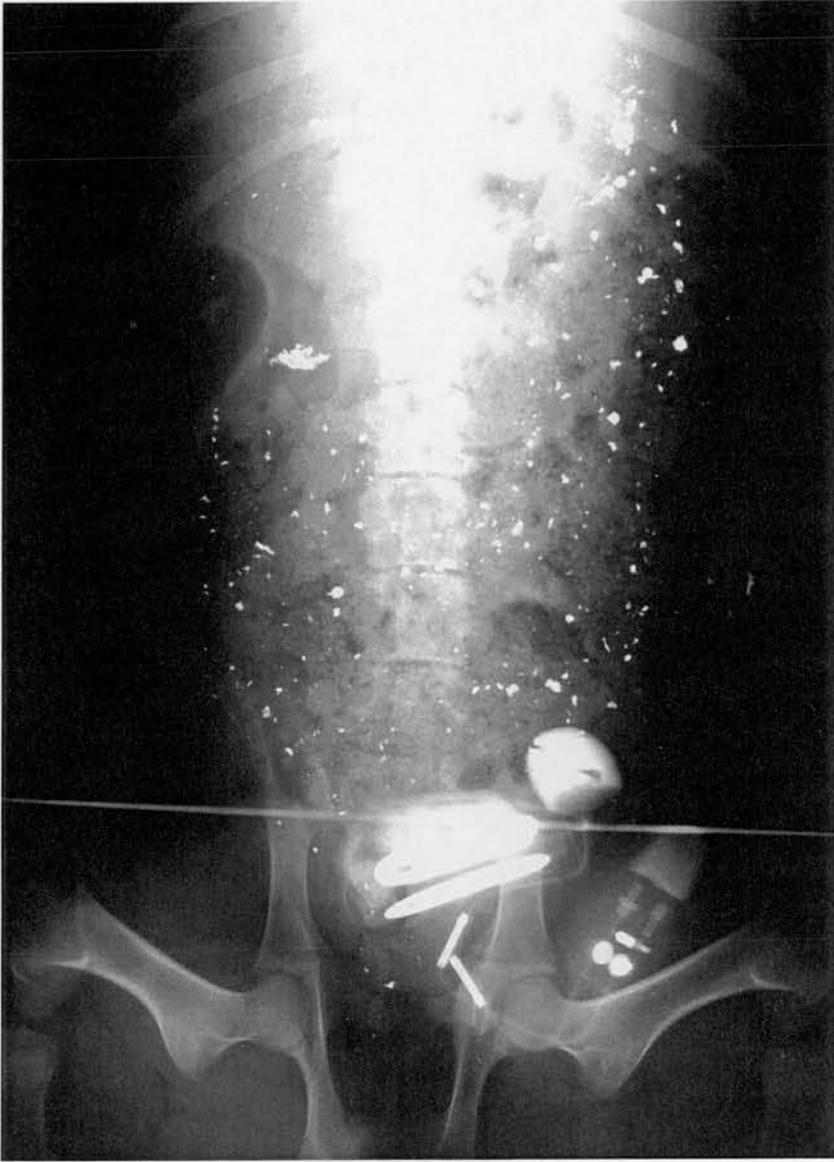


Figure 3: Markers disrupted by chewing on one occasion.

Chromic oxide ingestion study

The results of the chromic oxide ingestion transit studies are summarized in Figure 4 to Figure 7. Traces of chromium are detected in the stool within the first few hours and then the concentration declines. The concentration of chromium in the stools rises once again after approximately 20-24 hours in all animals and remains elevated at 30 hours. It also remained elevated at 50-55 hours in the two animals studied (Figure 5, Figure 7).

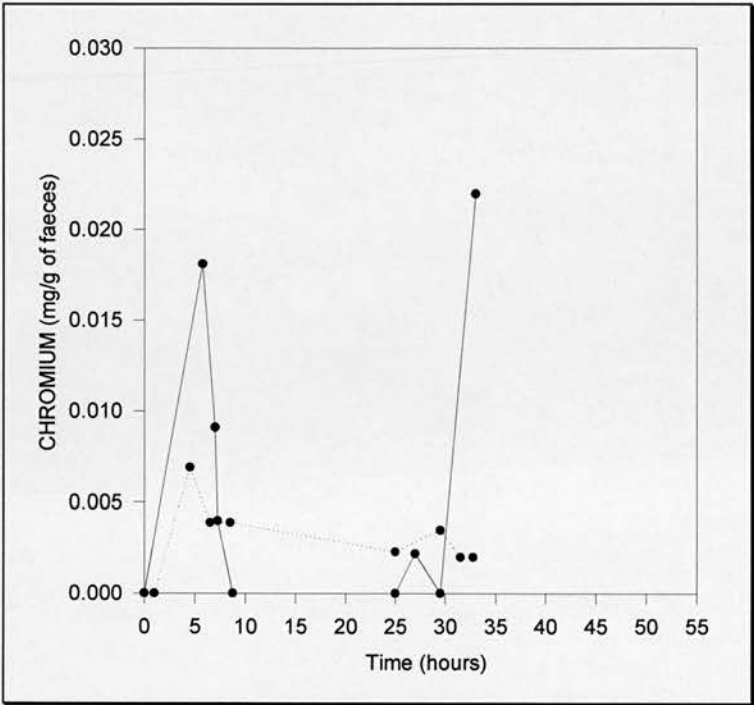


Figure 4: Unoperated animal (#20). Chromic oxide (1g) study on two occasions.

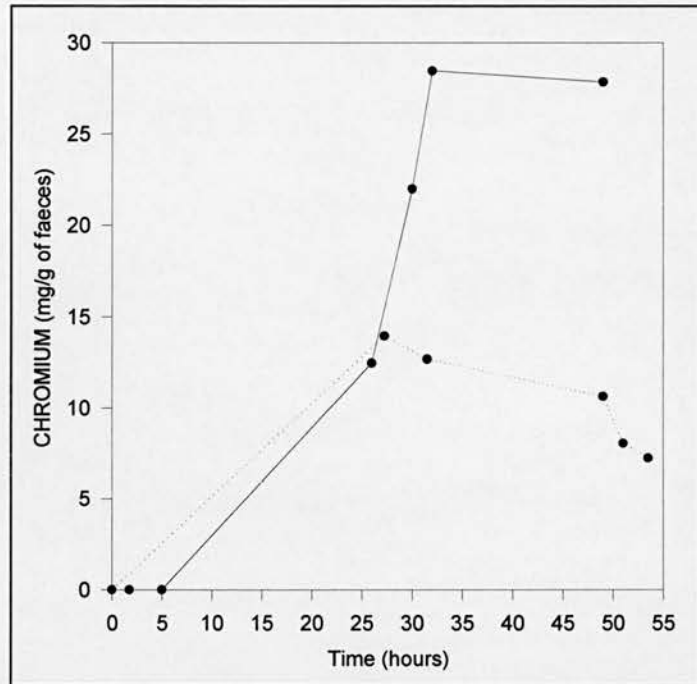


Figure 5: Unoperated animal (#20) Chromic oxide (10g) study.

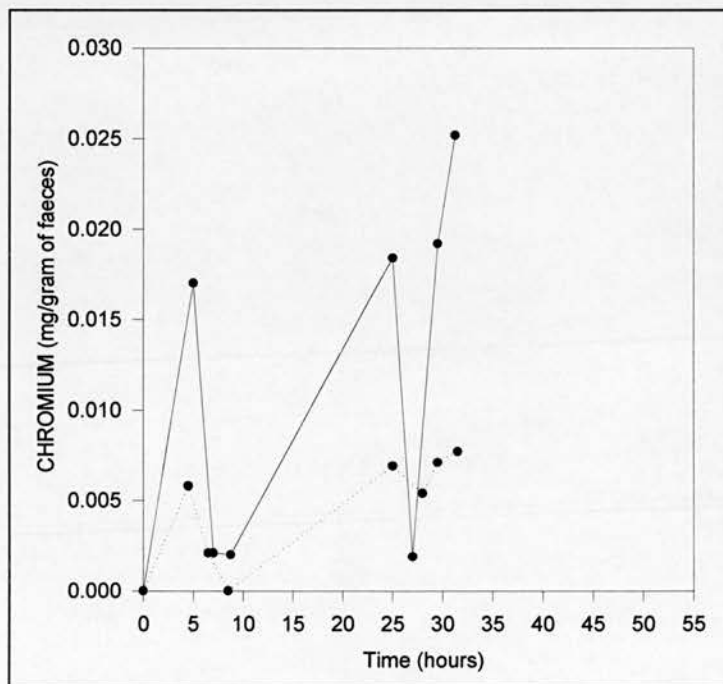


Figure 6: Unoperated animal (#19) Chromic oxide (1g) study.

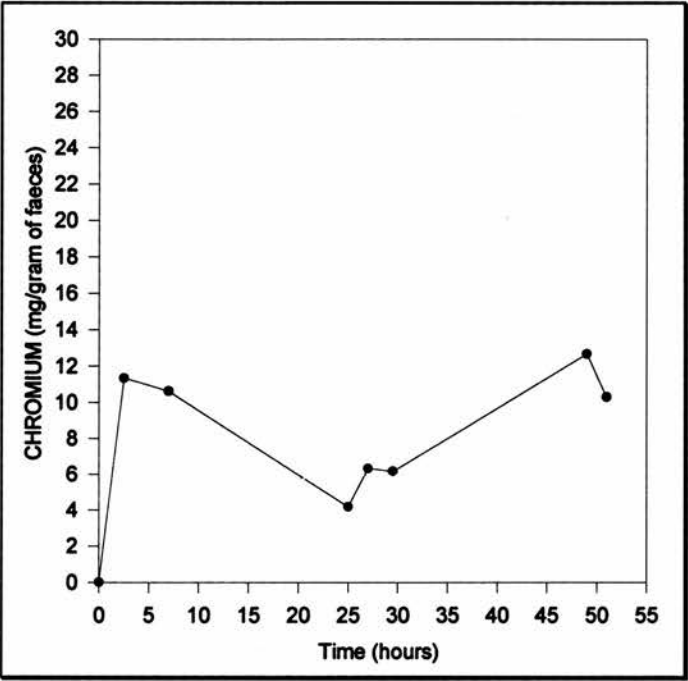


Figure 7: Chromic oxide (10g) study in animal with deactivated prosthesis (#16).

Discussion

This study was performed in order to obtain an indication of the duration of the colonic transit time in our experimental animals. The radiological method used³ in this experiment was recommended as the accepted standard by the working party on anorectal physiology measurement⁵. The original report by Hinton et al² involved daily X-rays for a minimum of five days. They reported that, in 25 healthy subjects, the first marker was passed within three days and that 80% of the markers had been passed by the fifth day. Our project license did not allow unlimited administration of general anaesthetics to the animals and since radiological evaluation could only be performed under anaesthetic or heavy sedation, the simplified method of Metcalf was preferred. The transit time in the unoperated animal was 21.6 and 36 hours and in the animals with the deactivated sphincter 13.6 and 28.8 hours, increasing to 43.2 hours upon activation of the device for six hours. Using the same method, the mean colonic transit time in healthy humans was reported to be 35 hours (S.E.=2.1)³ and 39 hours (S.E.=3)⁶. In contrast a much greater variability has been reported using Hinton's method^{1,2}: duplicate measurements varied by as much as three days¹ and transit time varied between 22 and 125 hours in males and 46 to 128 hours in females². Our results indicate that the transit time in the Yucatan minipig is comparable to that of humans. A transit time of six days (144 hours) has been reported for pigs⁷. This, however, was measured immediately post colonic resection and anastomosis and must be severely biased by the presence of post operative ileus and the effects of the anaesthetic and cannot be comparable to normal. Transit time does not appear to be markedly affected by the mere presence of this neosphincter, but is reportedly prolonged by 100% in enterectomised dogs⁸. In that study, however, the "artificial sphincter" reported by the authors consisted of two severely constricted non-relaxing myomecyomised segments of bowel.

Even though the above simplified radiological method can be used to estimate segmental transit times in the human colon, this was not possible in minipigs due to the differences in the colonic anatomy: the terminal ileum opens into the caecum which leads into the spiral colon. The two are superimposed in the right

and middle of the upper and lower abdomen. The spiral colon leads to a long rectum which spans the whole of the abdomen in a cranio-caudal direction (see Chapter 7) and there is no sigmoid colon. These colonic segments are superimposed making radiological evaluation of the segmental distribution of the markers impossible.

The magnitude of the transit time measured by the marker method is comparable to that measured by the chromic oxide ingestion/excretion method. Chromic oxide is not absorbed in significant quantities in the bowel and its appearance in the faeces marks the ingestion to anus time. The method for analysis used has been validated against a chemical assay method, and the inclusion of Calcium and Silicate in the standard solutions minimized extraneous interference⁴.

Traces of chromium are detected in the stool within the first few hours and then the concentration declines. This early rise is possibly due to contamination of the pen with the chromic powder. The concentration of chromium in the stools rises once again after approximately 20-24 hours in all animals and remains elevated at 30 hours. It also remained elevated at 50-53.5 hours in the two animals that this estimation was done (Figure 5, Figure 7).

In summary, the colonic transit time and mouth to anus time have been measured by two methods in a small number of our experimental animals. The transit time is comparable to that measured in healthy humans.

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Chapter 6

Survival animal experiments

This study was presented at the annual meeting of the Association of Surgeons of Great Britain and Ireland in London in June 1995 and was awarded the **Moynihan Prize** for 1995.

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Summary

A new implantable artificial anal sphincter in which an inflatable expander compresses and flattens the bowel against a pillow has been developed and tested in a porcine model. Sixteen animals were implanted and studied for periods of up to 20 weeks. Of the eleven animals where the artificial sphincter was regularly closed, eight completed the study and were continent during 85% of the activation times. There was no evidence of ischaemic injury.

Major complications were related only to the failure of the control pumps.

The study suggests that the neosphincter produces faecal continence without intestinal ischaemia. At present reliability is limited only by the performance of the pump.

Introduction

An artificial anal sphincter¹ (Chapter 3), which is designed to reproduce the normal physiology of the ano-rectum by flattening and angulating the bowel without causing crenation has been developed. The technical details pertaining to implantation in an animal model have been evaluated (Chapter 4). We have shown in the laboratory that by eliminating crenation, occlusion pressure was evenly distributed without localised high pressure points under the device (Chapter 3). Further, the design facilitates the creation of angulation of the bowel with a relatively large area of distribution of the occlusion pressure, allowing the device to be set at lower operating occlusion pressures than that required for circular designs yet still achieve continence.

In this chapter, the results of a study where this neosphincter has been implanted in a porcine model are presented.

Materials and Methods

The prosthetic sphincter consists of an inflatable expander which compresses the bowel against a gel-filled pillow (Figure 1).

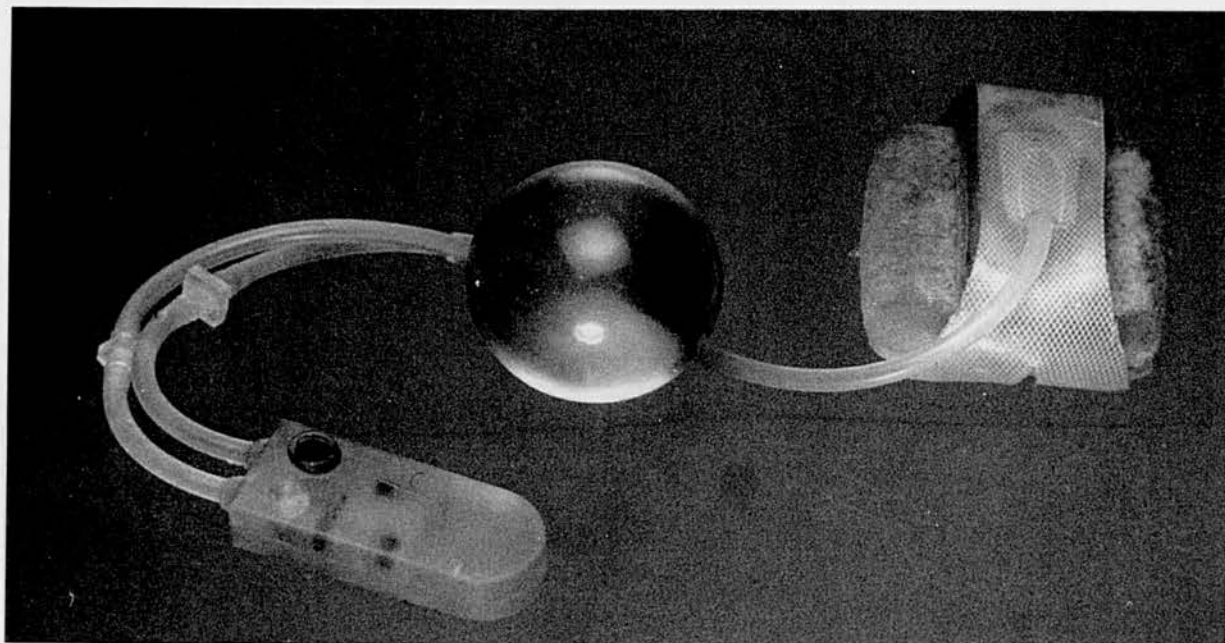


Figure 1: The implantable Neosphincter Prototype

A pressure regulating balloon maintains basal pressure in the expander at a value set between 65-120 cmH₂O. For defaecation to begin liquid is transferred from the expander to the balloon by means of a pump. When the expander is empty, the bowel is free to dilate which allows evacuation. Fluid then leaks back gradually to occlude the bowel over a 5 minute period. The pump incorporates a manually operated shut-off valve which allows the sphincter to remain open for prolonged periods (e.g. post-operative tissue healing). The neosphincter has been tested in a study of 16 female minipigs (weight 13.5-20 kg). Five of these animals were used as

controls (Group A): three were implanted but not activated, one had a sham operation and one had no surgery (Table 1). The remaining 11 animals (Group B) had implanted and activated sphincters.

	Number of animals	Type of operation
Group A (control)	5	No activation
Group B	11	Implanted, <i>activated</i>

Table 1: Details of the groups of the experimental animals.

The anal sphincters of all animals who underwent surgery were divided at the end of the implantation procedure.

Animals were observed for two to three weeks prior to surgery and bowel habit noted. During this period all animals were vaccinated against Salmonella with Bovivac (Hoechst Animal Health, Hoechst U.K. Ltd) 2 ml subcutaneously, two doses two weeks apart. Each animal was anaesthetised as described in Chapter 4. The peritoneal cavity was approached via a mid-line incision and the rectum was mobilised. In the implanted animals, the expander was placed beneath the lower rectum through a mesenteric window (Figure 2) and the pillow was positioned on the anterior surface of the bowel (Figure 3). The expander's tie straps were then threaded through the anchoring slots in the back of the pillow and the straps adjusted so that a 2.25 cm diameter cylindrical sizer could pass between the bowel wall and the neosphincter. The straps were then secured with Prolene sutures, apart from the first animal where vicryl was used. The pillow was sutured to the anterior abdominal wall. The uterus and fallopian tubes were used to cover the device, in order to avoid the development of intestinal adhesions.

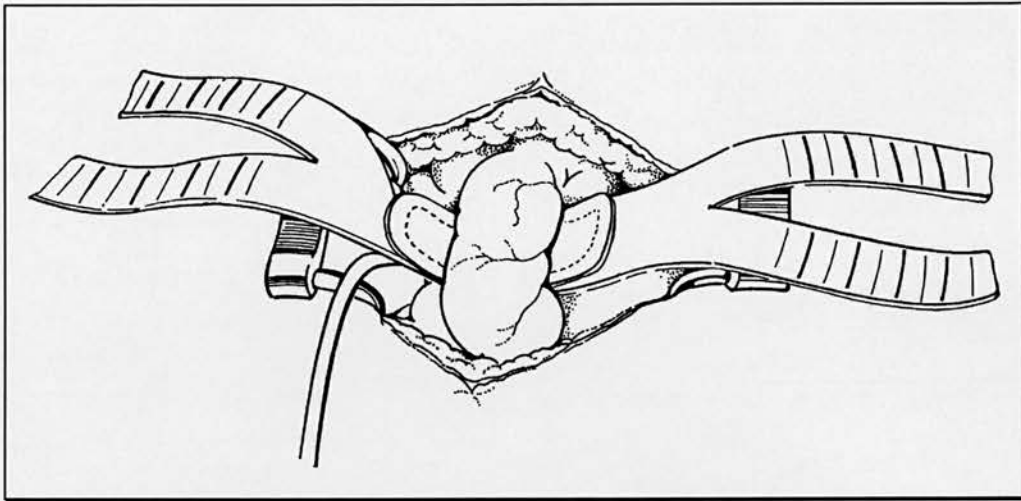


Figure 2: The expander is passed through a mesenteric window in the mesorectum.

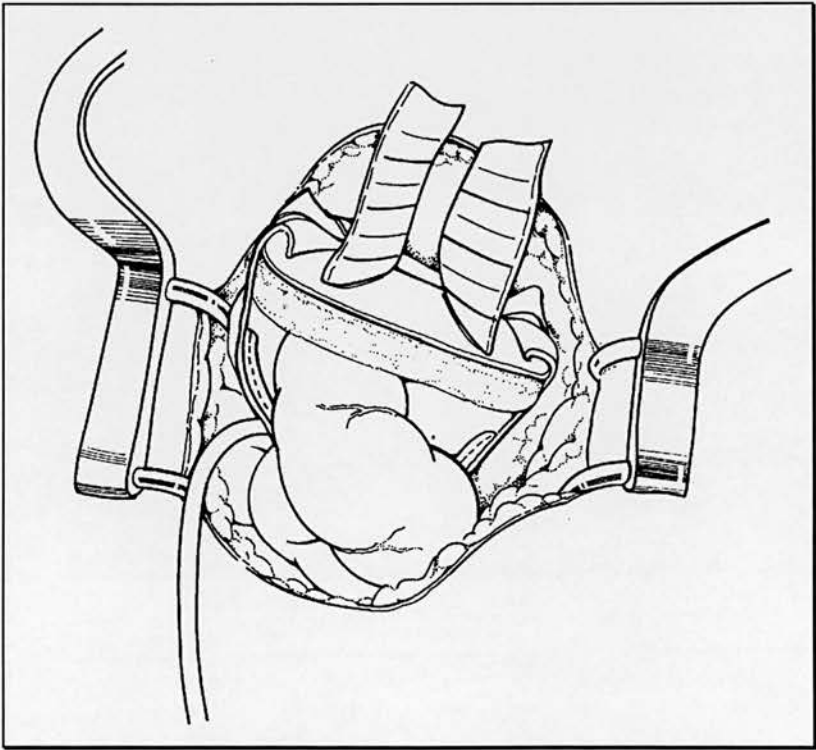


Figure 3: Appearance of the Neosphincter at the end of the implantation procedure.

The expander was then inflated with a 12.5% solution of Hypaque in normal saline until the intraluminal bowel pressure measured by a catheter tipped transducer (Type CTU1 Gaeltec Ltd, Isle of Skye) reached between 45-60 cmH₂O and the corresponding expander pressure noted. The balloon was placed in the peritoneal cavity and the control pump in the inguinal region through a subcutaneous tunnel. The pump and reservoir were primed with Hypaque solution and connected to the expander. The working pressure of the sphincter could be set to any level up to \approx 135 cmH₂O. The working pressure was set to the value found to give an intraluminal pressure (or operating pressure) of between 45-60 cmH₂O by adjusting the volume of liquid in the system. Pump function was checked and the expander then left deflated with the shut-off valve closed. All parts of the implant, the peritoneal cavity and the wound layers were copiously lavaged with a mixture of Gentamicin 0.8 mg/ml and Metronidazole 5 mg/ml. The wound was closed in layers with vicryl and interrupted Prolene to skin. The resting anal pressure was then measured using the station pullthrough technique. Finally, the anal sphincter of each animal was divided. Antibiotic prophylaxis (Ampicillin long acting 25mg/kg per day) commenced at induction and continued for one week after operation. Analgesia (0.01mg/kg Buprenorphine twelve hourly) was required for the first 24 hours post-op. The animals received a balanced electrolyte solution of Lactade (Beecham Animal Health) orally for the first 18 hours and resumed normal feeding thereafter. To avoid the risk of faecal impaction, all animals received a regime of mild laxatives (Liquid paraffin 15 ml once per day, Sterculia 98%, 5 ml twice per day). They were fed three times a day (commercial pig diet pellets, Stewart and Larbert Ltd, Larbert) and had free access to water. The sham operated animal underwent the same surgical procedure without the implantation of the prosthesis and the area of the mesenteric window was marked by non absorbable sutures.

After two weeks, to allow for tissue healing, each implanted animal was given a general anaesthetic and the sphincter closed by releasing the shut-off valve. 12.5% Hypaque was instilled into the rectum and the effectiveness of holdback by the sphincter demonstrated under X-Ray screening. Rectal angulation and the

position of the sphincter were measured from radiographs taken during screening. The resting anal pressure was measured once again using the station pullthrough technique.

The animals were housed in separate pens and the 11 implanted animals (group B) had their prosthetic sphincters activated for periods which gradually increased from 2 to 6 hours per day over a ten day period to allow intestinal adaptation. Pens were cleaned before each activation period and the animals were observed during the occlusion time for evidence of faecal soiling.

Continence was assessed and graded as follows:

- Grade I: Fully continent of formed faeces
- Grade II: Leakage solely within two hours of activation
- Grade III: Incontinent

If the sphincter was ineffective then sphincter pressure was increased by injecting more Hypaque solution into the system through the septum in the pumps. The animals in group B were variably terminated between 5 and 20 weeks post implantation in order to study the progressive effect of sphincteric compression on the bowel wall. All animals in group B had the sphincters continuously activated for 36 hours on at least three occasions one week prior to termination. Similarly, the animals in group A were terminated at between 11 and 18 weeks. Arterial blood pressure was measured by femoral artery puncture prior to termination.

At the time of termination, the implant was tested *in-situ* in four animals from group B, by inflating the expander to increasing volumes and recording the system pressure generated. The bowel surrounded by the prosthetic sphincter was excised with a further bowel sample from a region 10 cm proximal to the sphincter site. In seven animals, the colon was examined microscopically for necrosis and other host

responses. Haematoxylin and Eosin sections were taken from seven of the eight implanted and activated animals and the average mucosal thickness was estimated by measurement from five different areas using a traveling microscope (magnification $\times 400$). The bowel width and wall thickness was also measured macroscopically.

Results

Of the 16 animals studied three were terminated within two weeks and did not provide data regarding neosphincter function. One of these three had an early implant infection; the remaining two developed colonic obstruction (one due to control pump malfunction which caused the sphincter to remain closed, the second due to a misaligned expander). There were, therefore, five animals in Group A and eight animals in Group B available for long term study.

At two weeks, radiological evaluation of the device in each implanted animal demonstrated holdback for fluids confirming activation (Figure 4). The mean angle created by the device at that time was 61° (S.D.=20.93), while the mean distance of the prosthesis from the anus was 18.5 cm (S.D.=4.22). The resting anal pressure fell from 20.8 mmHg (S.D.=5.9) prior to division of the anal sphincter to 0.4 mmHg (S.D.=1.4). This was statistically significant ($p<0.001$, $T=15.8$, d.f.=34). Arterial blood pressure was 72/51.8 (10.9/8.5)mmHg (mean systolic/diastolic, S.D. in brackets). Blood pressure was not significantly different when compared with that of the animals used in the acute experiments (systolic: $p>0.13$, diastolic $p>0.80$, Chapter 4).

The observation of bowel frequency undertaken before surgery showed that the mean rate of defaecation was 8.6 times/24 hours (S.D.=3.26). In the sham operated control animal this increased to a mean of 20.1 times/24 hours (S.D.=3.69) after surgery. In the 3 implanted but non-activated controls the corresponding defaecation frequency was 13.4 times/24 hours. The mean defaecation frequency of all five control animals (group A) was 14.1 times/24 hours (S.D.=5.45), i.e. equivalent to once every 1.7 hours. Details of the post operative continence in the 8 animals with activated sphincters after surgery (group B) are shown in Table 2. The animals were completely continent of faeces during 75% of the activation times (Table 2 continence score I). Soiling during the first 2 hours of the 6 hour occlusion period occurred 9% of the time. The animals were incontinent during 15% of the occlusion times.

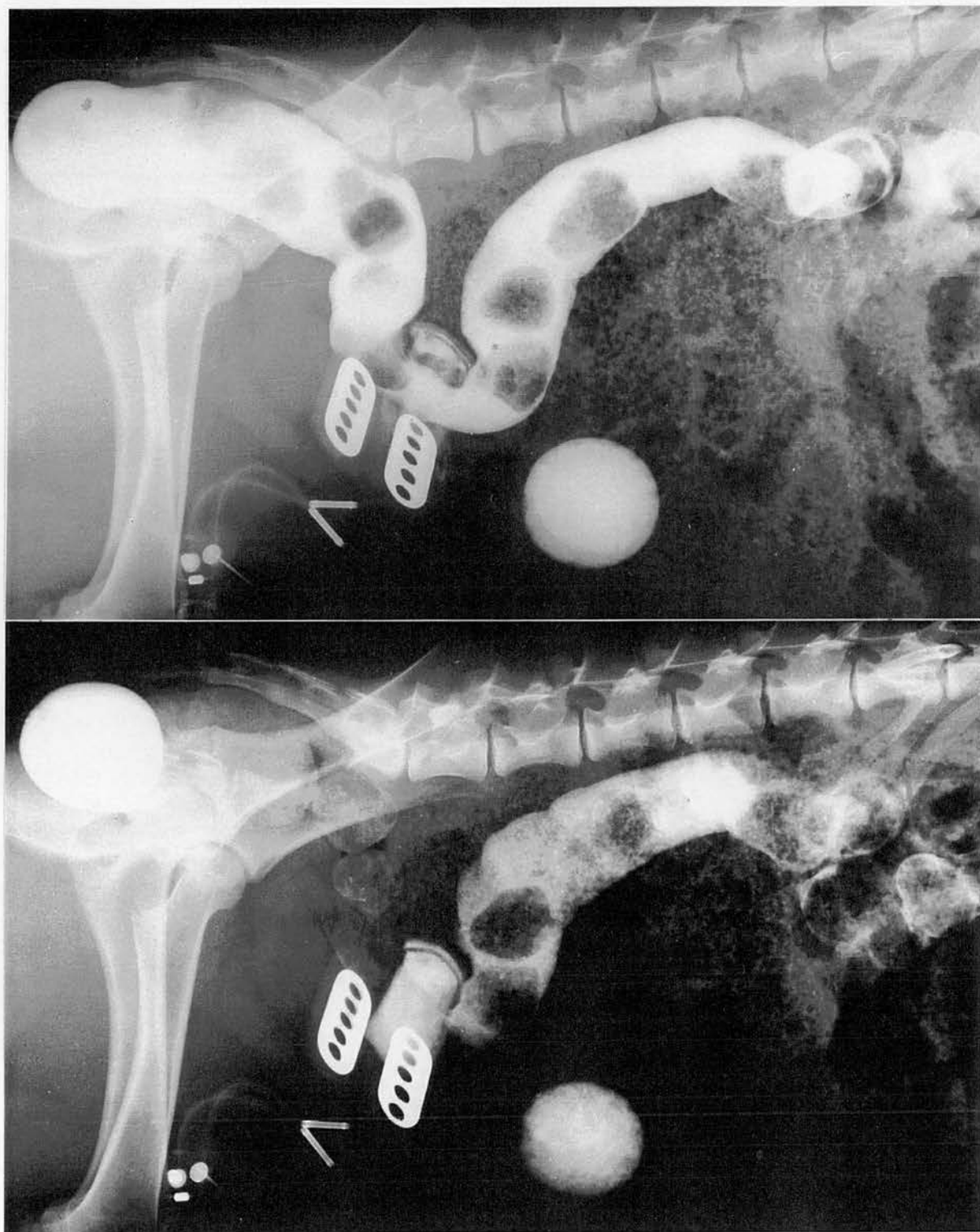


Figure 4: Radiological appearance of the artificial sphincter after instillation of contrast material in the rectum (top). The neosphincter is activated and the distal rectum cleared to demonstrate effective fluid holdback and bowel angulation (bottom).

Active implant duration (weeks)	Bowel angulation	Operating occlusion pressure (cmH ₂ O)	Number of activations of 6 hours in lifetime	Number of occasions each continence score was observed during the activation periods. CONTINENCE SCORE:		
				I	II	III
5	50°	51	5	5	0	0
7	65°	45	3	2	0	1
8	80°	46	6	4	1	1
9	75°	46	15	10	1	4
10	40°	60	4	1	3	0
15	65°	43	38	33	2	3
18	85°	41	52	33	5	14
20	40°	64	38	33	4	1
		Total:	161	121 (75.2%)	16 (9.9%)	24 (14.9%)

Table 2: Continence data for Group B animals with activated sphincter.

Continence score:

- I. Continent of formed faeces
- II. Leakage solely within two hours of activation
- III. Incontinent.

During follow up of the 13 animals, there were six pump malfunctions: four had leaking shut-off valves, one developed a blocked bypass resistor and one pump casing developed leakage of fluid. The only problem associated with the active sphincter, related to the use of vicryl for the expander anchoring sutures which allowed the expander to dislodge from the pillow in one animal.

At post mortem it was noted that a fibrous capsule had formed around each prosthesis. The pressure-volume relationship was studied in detail in four sphincters *in-situ* as shown in Figure 5. The compliance of the sphincter complex is represented by the slope of each point of each curve (compliance $C=\Delta V/\Delta P$) in Figure 5 and is reduced in all animals. There was no definite progressive loss of compliance with time.

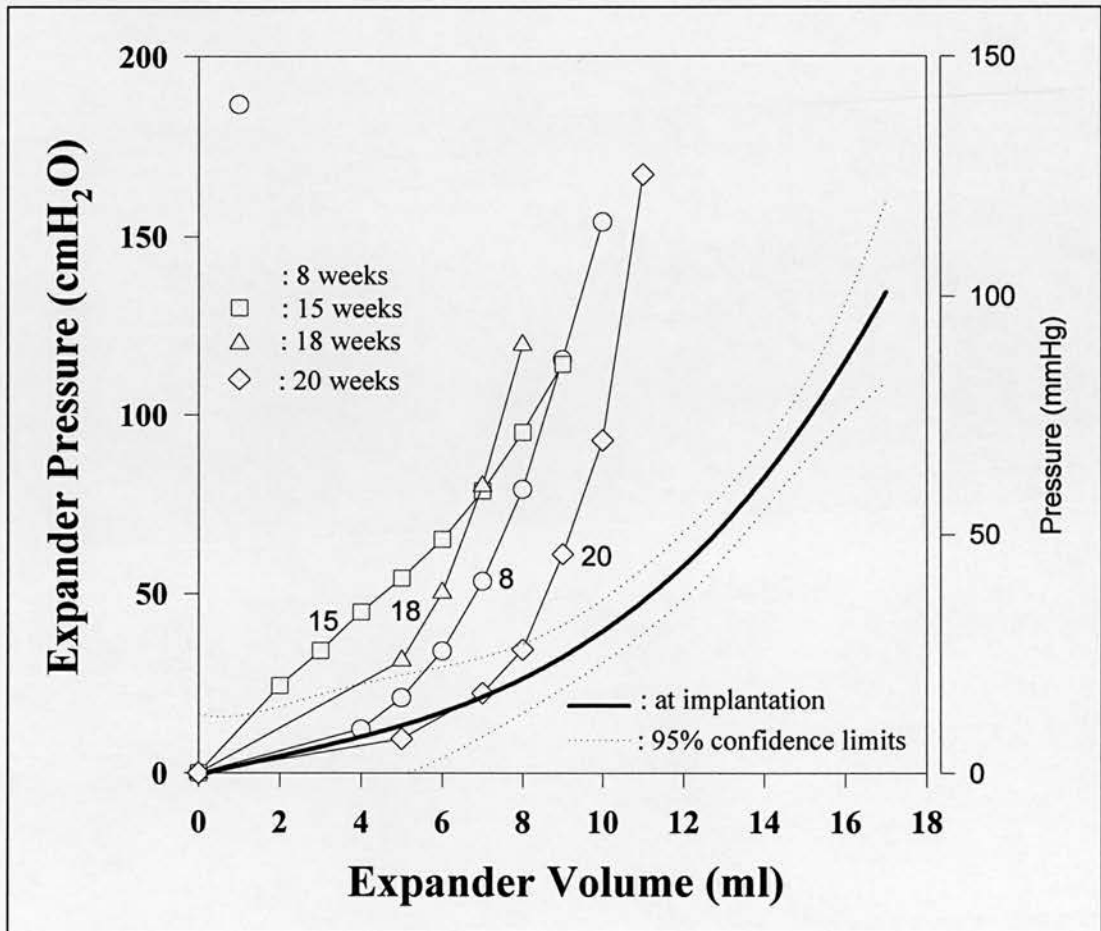


Figure 5: Expander Pressure *versus* Volume at implantation and at post-mortem in four implanted and activated animals.

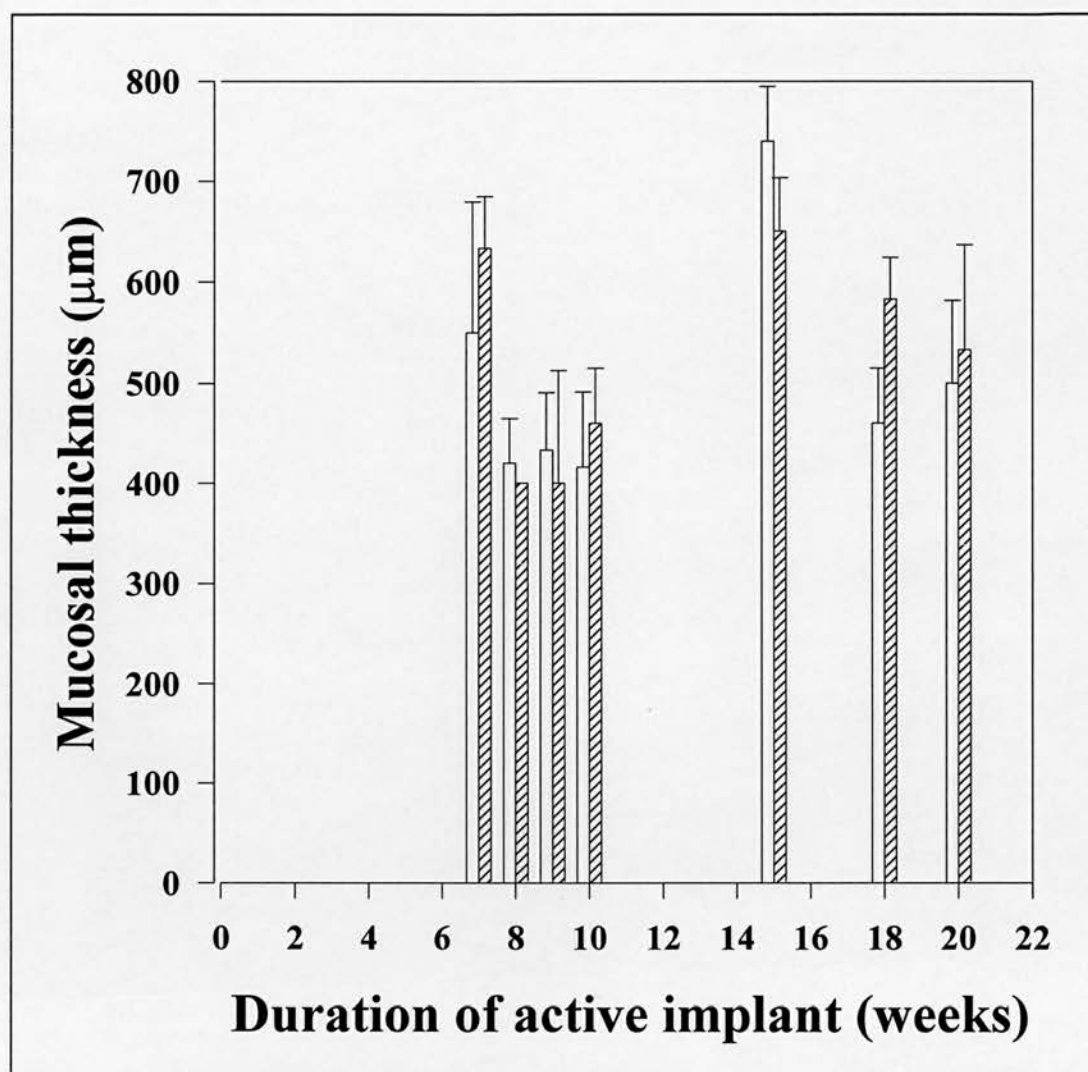


Figure 6: Mucosal thickness *proximal to the sphincter* (no fill) and *under the sphincter* (diagonal fill) for seven implanted and activated animals. Bars represent mean + Standard Deviation.

Histological examination of tissues underneath the prosthesis showed no evidence of rectal ulceration. The average mucosal thickness in the control animals was 445 μm (S.E.M.=37.8). The mucosal thickness proximal to the sphincter in the activated animals was 502.7 μm (S.E.M.=115.2) and at the sphincter site 522.8 μm (S.E.M.=105). There was no significant difference between the mucosal thickness in the seven sets of specimens taken proximal to the sphincter and those from under the sphincter ($p=0.49$) (Figure 6). There was also no significant difference between the

mucosal thickness of the controls and that of the mucosa proximal to ($p=0.36$) or at the sphincter site ($p=0.19$) in the activated animals. All rectal layers were well preserved apart from the loose areolar tissue of the submucosa (Figure 7). There was a slight but significant dilatation of the rectum proximal to the sphincter and also thickening of the bowel wall both in the proximal and distal rectum. These changes were due to muscle and serosal thickening (see Appendix 5). Silicone deposits were not identified in any of the specimens.



Figure 7: Histological appearance of rectal wall at the level of the neosphincter, showing preservation of mural elements and compression of the loose areolar tissue

Discussion

The results of the present study confirm the efficacy of the neosphincter design. The implant was at least 75% effective in achieving continence, while there was no clinical or histological evidence of ischaemia in the colon beneath or adjacent to the implant. This is in contrast to the mucosal atrophy which was observed when a circular cuff design was implanted around bowel² and stomach³ in dogs and in pig colon⁴. Significant urethral atrophy was also observed under the AMS 800 cuff in piglets (male more severe than females) within six to eight weeks of implantation⁵, even though the device was never activated.

The mini-pig was chosen as the experimental model because the size, structure and biomechanical properties of the intestine^{6,7}, and the dietary composition and consistency of faeces⁸ are similar to that of humans. Colonic transit time is also similar to that of humans (Chapter 5). Since it has been observed that mini-pigs⁹ and dogs² in the laboratory setting readily obstruct with viscous stools, a gentle laxative regime was used to avoid this possibility. Mini-pigs also have a more frequent defaecatory pattern than humans. Our control animals evacuated approximately every two hours imposing a limit on the maximum occlusion time of six hours. This maintained animal comfort but challenged the neosphincter to hold back the volume of three motions. This would equate to an occlusion time of at least 24 hours in the human. We have also shown that the sphincter does not cause ischaemic changes, even when it was activated for 36 hours in the minipig. The duration of activation is in accordance with other studies: a period of six hours was reported in a mongrel dog model¹⁰, six to eight in beagles^{2,11} and three to eight in a porcine ileostomy model¹². An occlusion period of 23 hours in pigs with a perineal colostomy caused bowel erosion in almost 100% of animals⁴.

The prototype sphincters used in the present study were of a size suitable for human implantation and as such were too large to place in the porcine pelvis. This dictated that the occlusion site was on average 18 cm from the anus. Such placement had the disadvantage of potential evacuation of faeces from the lower rectum after

neosphincter activation. For this reason we have separately documented animal continence for the whole activation period and episodes of incontinence during the first two hours after activation (see Table 2). Where some evacuation occurred during the first two hours, but the animals were continent thereafter, it seems probable that this resulted from emptying of the dead space. The two hour interval was chosen to be just greater than the average defaecation frequency expected in the control animals. Taking this into account, it appears that the device was successful in achieving continence 85% of the activation time. Animals were unequivocally incontinent for 15% of the activation times. Loss of fluid from the system accounted for seven episodes of faecal incontinence in one animal (29% of the total episodes of incontinence in all animals). This problem was rectified by injection of fluid into the hydraulic system. The other major cause of incontinence was the separation of the two components of the device (expander, pillow) due to re-absorption of the vicryl sutures used to secure the straps in the first animals. This was corrected by using non-absorbable sutures in the remaining animals.

Silicone shedding¹³ was reported in 50% of children with the artificial urinary sphincter after three years. No silicone particles have been observed histologically in our study, but remains a possibility after long term implantation. Encapsulation has been observed around all silicone implants including the circular urinary cuff sphincter^{2,4,9,14}. We found that encapsulation also occurred around our neosphincter making the expander less compliant with the potential risk of impairing pressure transmission. The surface of our neosphincter was textured, to minimize the effect of capsule formation, as texturing promotes the development of a more compliant capsule¹⁵. It is recognised that the elastic properties of these capsules change as they mature and may account for the variation in compliance that we measured with time. Certainly we observed no progressive loss of compliance with increasing implantation time (Figure 5). The materials used for the present sphincter are of a similar grade to those used in the urinary sphincter which had a lifespan of more than ten years. It is reasonable to assume, therefore, that comparable compliance changes and lifetimes should be expected for the present device.

Complications encountered in the present study were predominantly due to the unreliability of the pump. In particular, shut-off valve leakage led to prolonged unplanned sphincter activation and was responsible for obstruction in three animals. This pump, which was developed in our laboratory, is undergoing redesign before implantation in humans. The engineering tolerances expected from these pumps will be very high, and cycling apparatus has been designed to assess continuing reliability after several tens of thousands cycles of activation (equivalent to approximately 50 years normal usage). It may be that the automatic re-occlusion feature used in the urinary device will not be appropriate for the more prolonged act of defaecation, and the new design includes an option of keeping the sphincter open until defaecation is complete.

The key design feature of our sphincter is the inclusion of angulation with flattening of the bowel which reduces the occlusion pressure necessary to control formed stool. This is in accordance with our present understanding of the dynamics of flow and has been confirmed in our laboratory studies¹⁶. As in the human sphincter the device will be less effective in controlling liquid. Using the current design, we were able to achieve continence at occlusion pressures of only 45-60 cmH₂O. The angulation in this study was created in the upper rectum some 18 cm from the pelvic floor. In the human we expect to place the device at the level of the upper anal canal above the pelvic floor, after rectal mobilisation. Assuming similar angulation of the anorectal angle is achieved in the human, we would expect to operate the system at an occlusion pressure of 65 cmH₂O. This is the lower level of normality for basal anal canal pressures and a level at which we have shown there is no risk to the blood supply of the human colon (Chapter 8). Transient rises in intra-abdominal pressure will produce transient rises in hydraulic system pressure; a further benefit of the design.

In conclusion, this study has shown that our novel prosthetic anal sphincter produces continence without tissue damage in the minipig model.

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Chapter 7

Radiological evaluation of the Artificial anal Sphincter

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Introduction

There are several reports outlining the radiological evaluation of the several models of the artificial urethral sphincter prosthesis¹⁻⁷ and also the AMS 800 during its use as an artificial anal sphincter⁸⁻¹¹.

The design, operation and implantation of the AASP 2000 artificial anal sphincter has been described in previous chapters (Chapter 3, Chapter 6). As the device is fully implantable, clinical assessment -especially in a less than fully cooperative animal- could be at best difficult. Even under the best possible circumstances clinical assessment would be inconclusive in a significant proportion of malfunction episodes, and radiological assessment would, therefore, be necessary to contribute to the further elucidation of each problem. As this system is filled with radioopaque contrast material, it is particularly suited to radiological assessment. The radiographic techniques used to evaluate patients with sphincters are not new, and no special equipment is necessary. This chapter outlines the methods used to assess a malfunctioning device and presents a logical algorithm to assist with the diagnosis and management of these malfunctions.

Materials and Methods

A short, *in-vitro*, study was performed to evaluate the appearance of the components of the AMS and AASP control pumps (Figure 1, Figure 2, Figure 3). The pumps were filled with Hypaque solution and X-Rayed on the bench with the shutoff valve open (deactivated) and closed (activated).

The animals were routinely X-rayed two weeks after implantation to assess and activate the device. They were also X-rayed whenever a complication arose. This was performed under Halothane face mask anaesthesia (technique as described in Chapter 6, but without endotracheal intubation). The project license allowed for repeated sedation / anaesthesia for radiological assessment for therapeutic reasons.

Plain X-Rays were taken in the ventrodorsal (Figure 4) and lateral shoot-through planes (Figure 5) with the animal lying in a radiolucent gutter. The distance between the plate and the X-Ray head was kept constant throughout the duration of the study to ensure that size measurements were compatible between investigations.

The activation and deactivation of the device and effective fluid holdback were also assessed by a contrast enema.

Activation of the neosphincter

In most animals the device was left unprimed and was activated after two weeks in order to eliminate the risk of inadvertent activation during the post-operative recovery phase. A dose of Amphipen (Appendix 6) was administered with the pre-medication and another dose was given 24 hours later. Under a general anaesthetic, the injection port of the pump was impaled under strict asepsis (Figure 6) and a solution of Hypaque in saline (as described in Chapter 6) was instilled through a three way tap. When filled with radioopaque fluid, the expander, tubing, balloon reservoir and control pump are readily identifiable (Figure 4). This also allowed simultaneous measurement of the hydraulic system pressure; the pressure was set to the desired level (≈ 65 mmHg) by the infusion of the appropriate volume of fluid.

Hydraulic system pressure measurements were made using a Baxter pressure transducer (Uniflow DPT model).

Anal tone was measured during the anaesthetic sessions by the station pullthrough technique with a catheter tipped microtransducer (Gaeltec CTU1, see Chapter 1, Chapter 3, Chapter 6).

Demonstrating fluid holdback

A Foley catheter was inserted in the rectum and the balloon filled with 30 ml Hypaque solution. 100-200 ml of Hypaque (diluted as above), was quickly instilled into the rectum and an X-Ray was taken (Figure 7). Gentle traction on the catheter ensured that the anal canal remained sealed. The neosphincter was then activated and the distal rectum washed using copious amounts of saline in order to remove the contrast material. Another X-Ray was taken in order to demonstrate effective fluid holdback (Figure 8). The device was then deactivated and the animal allowed to recover.

The anorectal angle and the distance of the neosphincter from the anal margin was also determined from these radiographs. The latter was calculated after correction for projection enlargement was applied.

Assessment of the hydraulic switch

The silicone casing of the switch was impaled percutaneously with a #25 needle (Figure 6) and the pressure inside the casing measured. Hypaque solution was instilled to outline the switch and the tubing if necessary, e.g. if vacuum had developed inside the casing (Chapter 3 and subsequent discussion).

Results

***In-vitro* study of the pump components**

The AMS pump was X-Rayed in two planes (Figure 1, Figure 2) to show its components (Figure 1) and assess the shutoff valve travel (Figure 2).

The travel of the AMS pump shutoff valve (Figure 2) was three times that of the AASP device (Figure 3). The inner voids of the former were also much neater and of an overall greater diameter despite its smaller overall size.

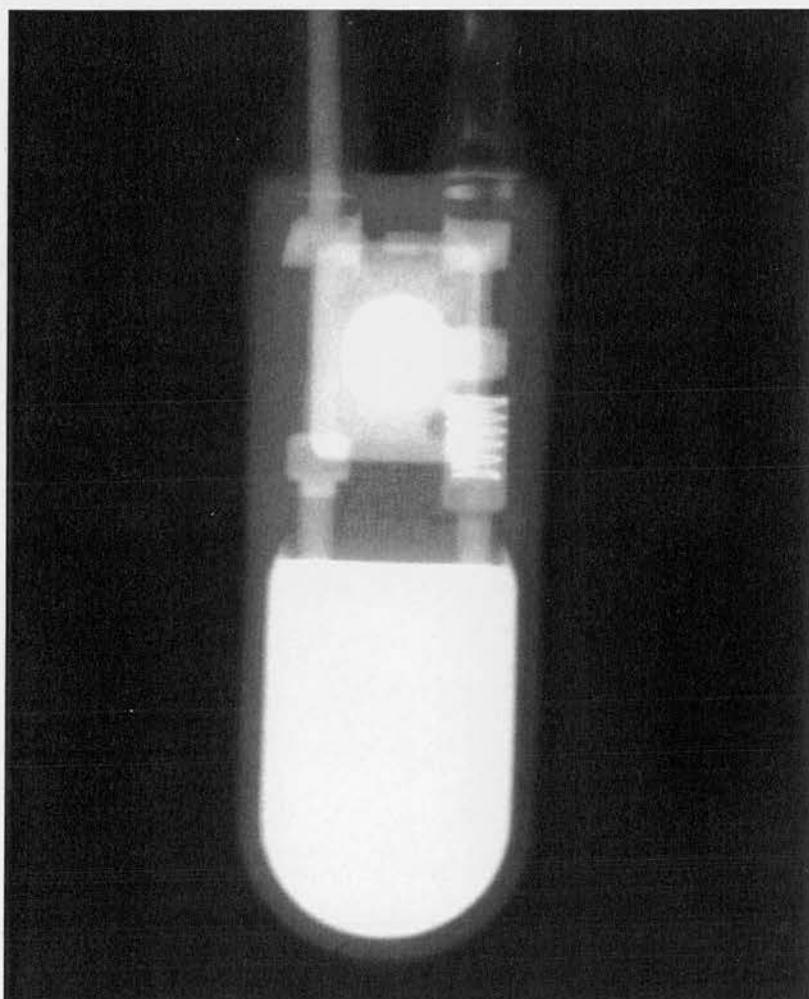


Figure 1: Vertical (PA) view of the AMS pump showing the spring loaded ball valve on the balloon side and its non-spring loaded counterpart on the sphincter cuff side. The shutoff valve (radioopaque circle) is also shown.

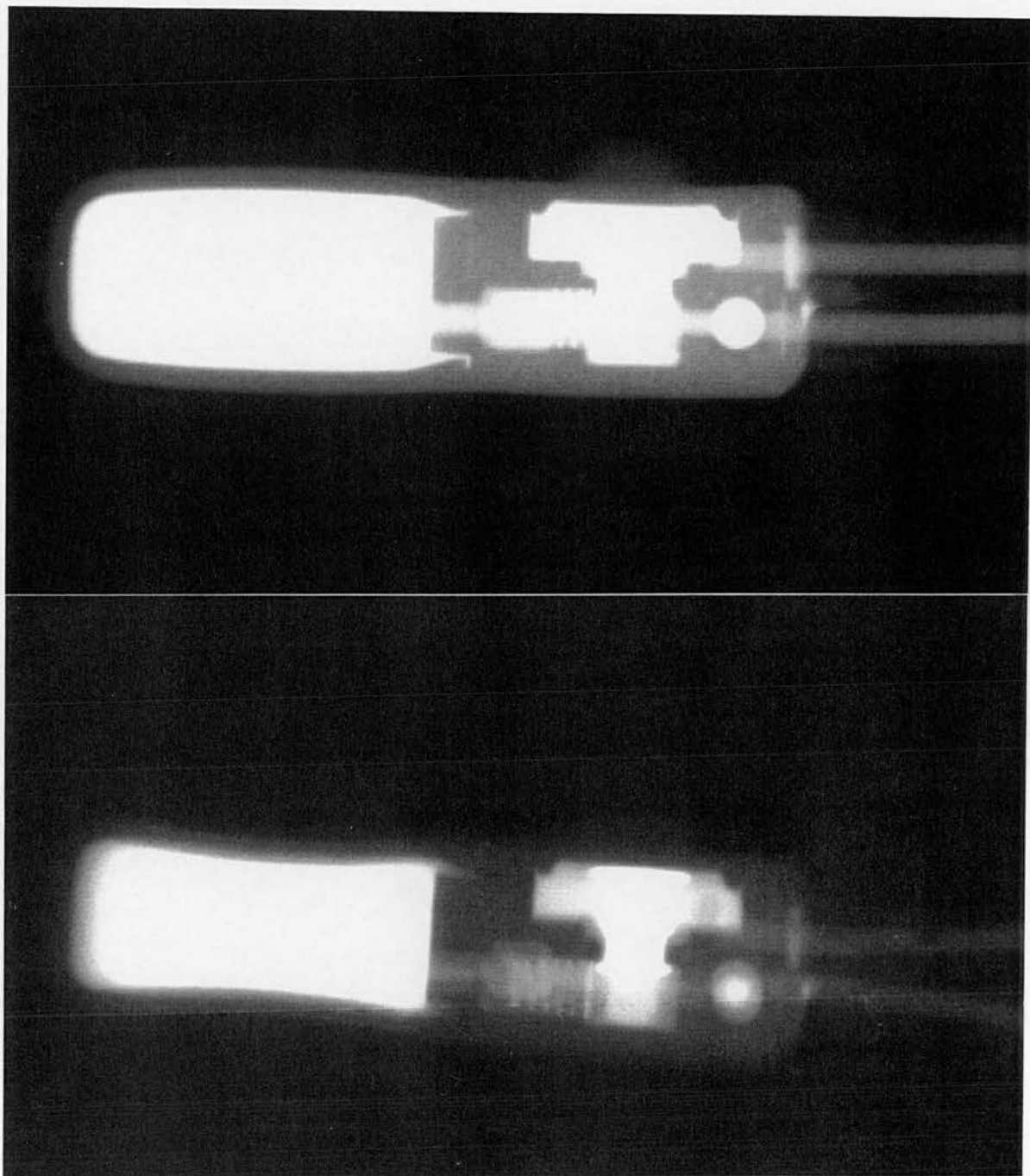


Figure 2: Lateral exposure of the AMS pump with the shutoff valve closed (top) and open (bottom). Valve travel is approximately 9 mm on projection.

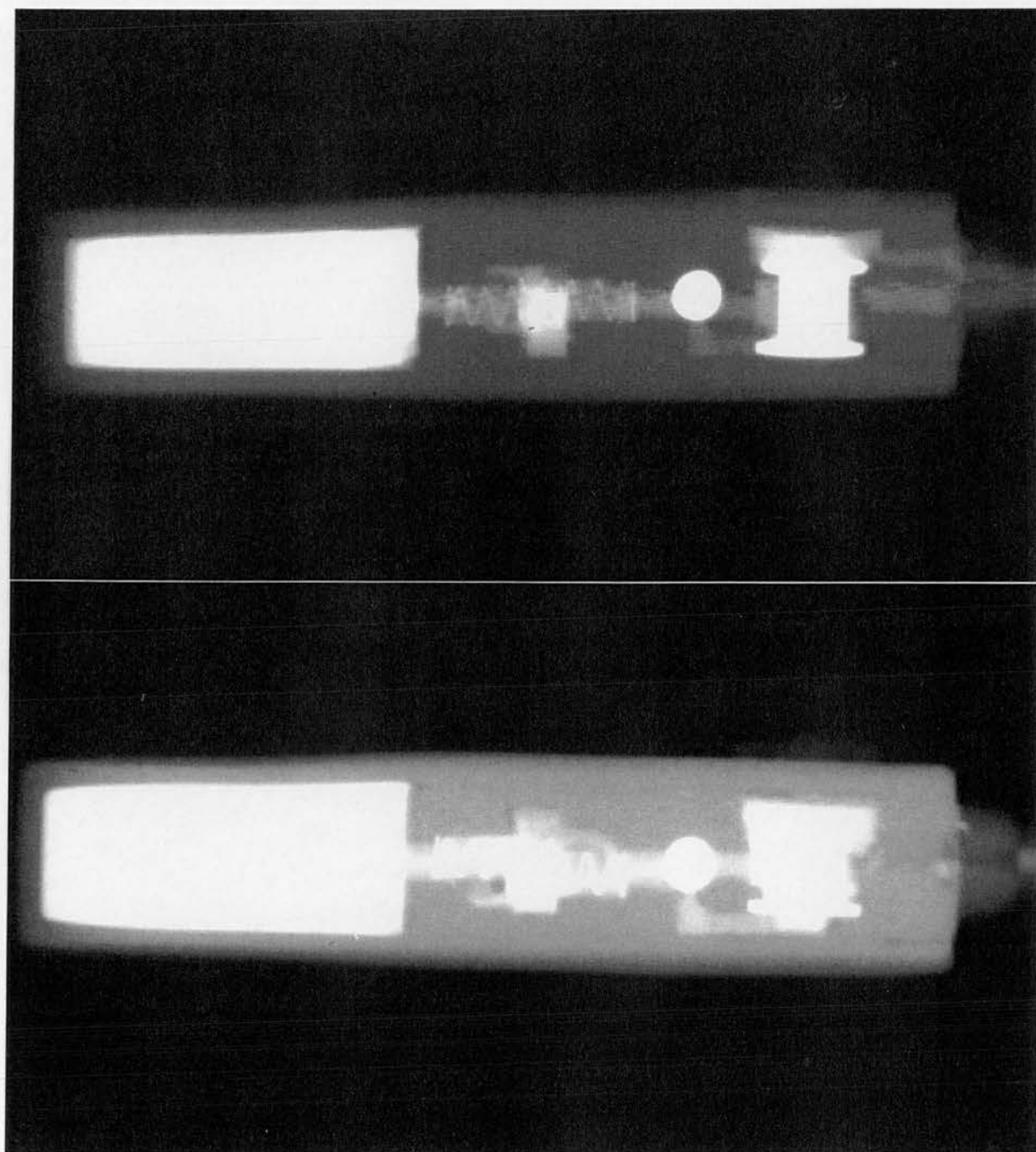


Figure 3: Lateral exposure of the AASP pump with the shutoff valve closed (top) and open (bottom). Valve travel is approximately 2.5 mm on projection.

***In-vivo* radiological studies**

There were no complications attributable to the performance of these investigations.

Anatomical positioning and assessment of function of the neosphincter

The position of the device, the normal appearances of its components and the anatomy of the bowel on plain radiography and after contrast instillation are shown in Figures 4 to 9. The components of the pump (shutoff valve, resistor, spring loaded one way valves and injection port backing plate) are clearly seen. In Figure 7 and Figure 8 the satisfactory performance of the neosphincter is confirmed by demonstrating effective fluid holdback.

The internal components of the optional hydraulic switch are shown in Figure 9. As it can be seen, this switch consists simply of an encapsulated spring type hose clip with a ratchet type catch. The contour of the switch can be palpated through the very thin silicone casing and manual opening or closing can be effected as appropriate.

The ventrodorsal view demonstrates the anatomy of the porcine distal large intestine after contrast instillation (Figure 10). There is no sigmoid colon in the pig (in fact there is no anorectal angulation either as this is only a feature of man and orthognate apes), and the rectum is seen to extend to the splenic area. This was also confirmed at laparotomy.

The AMS 800 pump was implanted in one animal (Figure 11). This device has a very reliable shutoff valve, but it has no injection port and its casing is not self sealing. As system pressure measurement was an essential part of the experimental protocol, an injection reservoir was implanted in the circuit to provide percutaneous access to the system (Figure 11 and Figure 12).



Figure 4: Ventrodorsal view of the primed but deactivated device. The intraperitoneal balloon is seen in the right mid abdomen, the control pump in the left inguinal region and the (optional) shunt and series switches in the right and left inguinal regions respectively. The contour of the empty expander is seen, partly covered by the steel reinforcing plates of the pillow.



Figure 5: Lateral shoot-through view of the activated device. The two segments of the filled expander are seen just being separated from the pillow by the colon, which is compressed by the activated expander.



Figure 6: Crop view of the control pump with a #21 needle impaling the injection port. The shutoff valve, resistor and spring loaded one way ball valves are also shown.

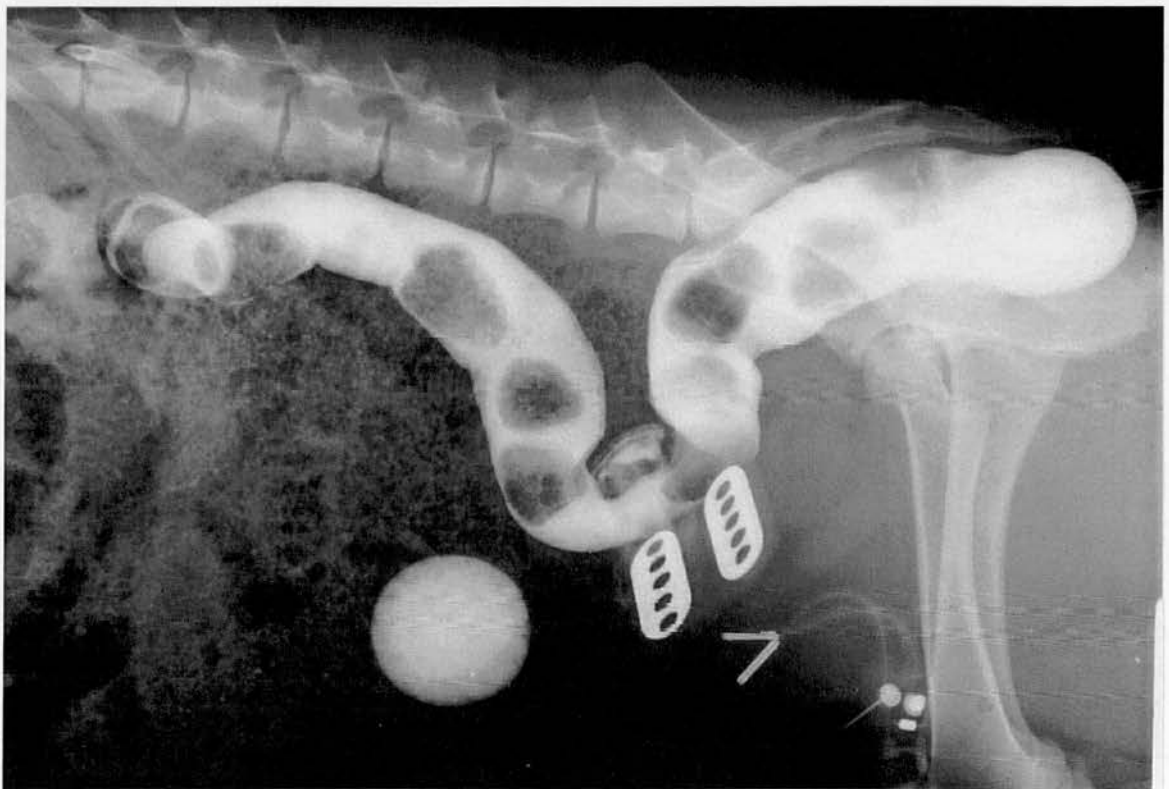


Figure 7: Contrast outlines the bowel with the device deactivated.

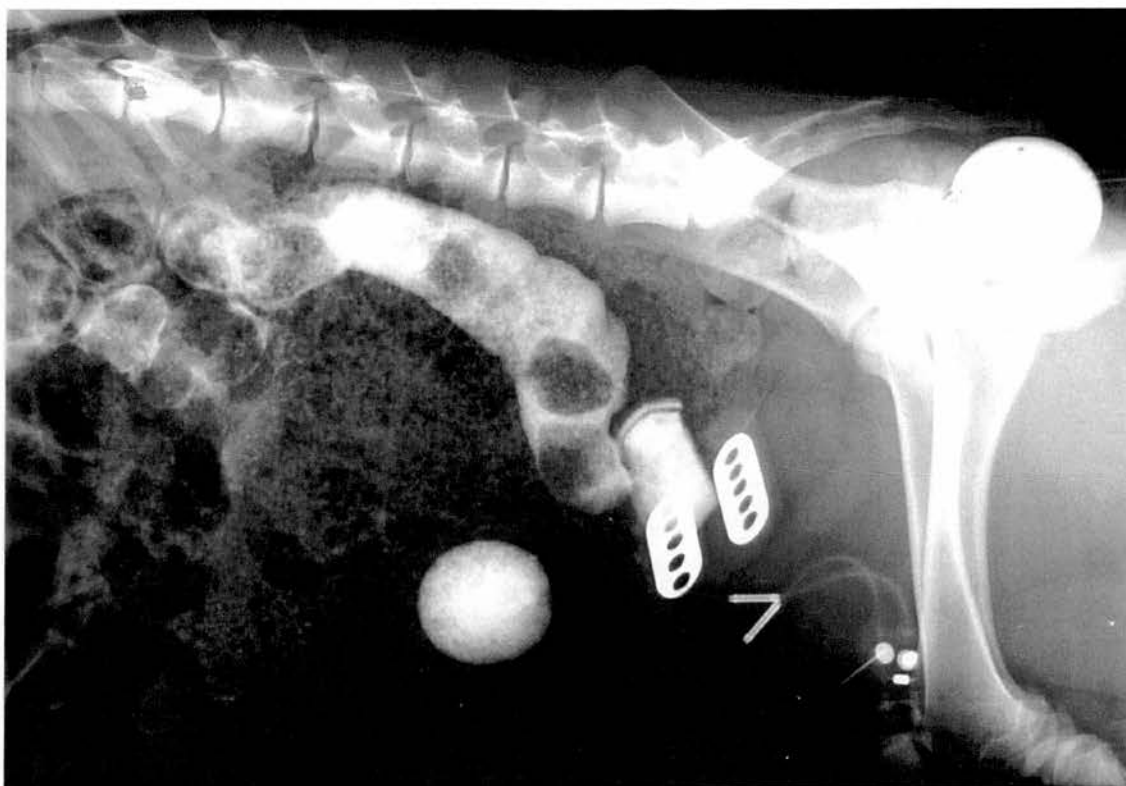


Figure 8: The Neosphincter is activated and the rectum cleared demonstrating fluid holdback.



Figure 9: Lateral shoot through X-Ray of the unprimed, deactivated device. The switch casing has been filled with contrast to show the outline of its components.

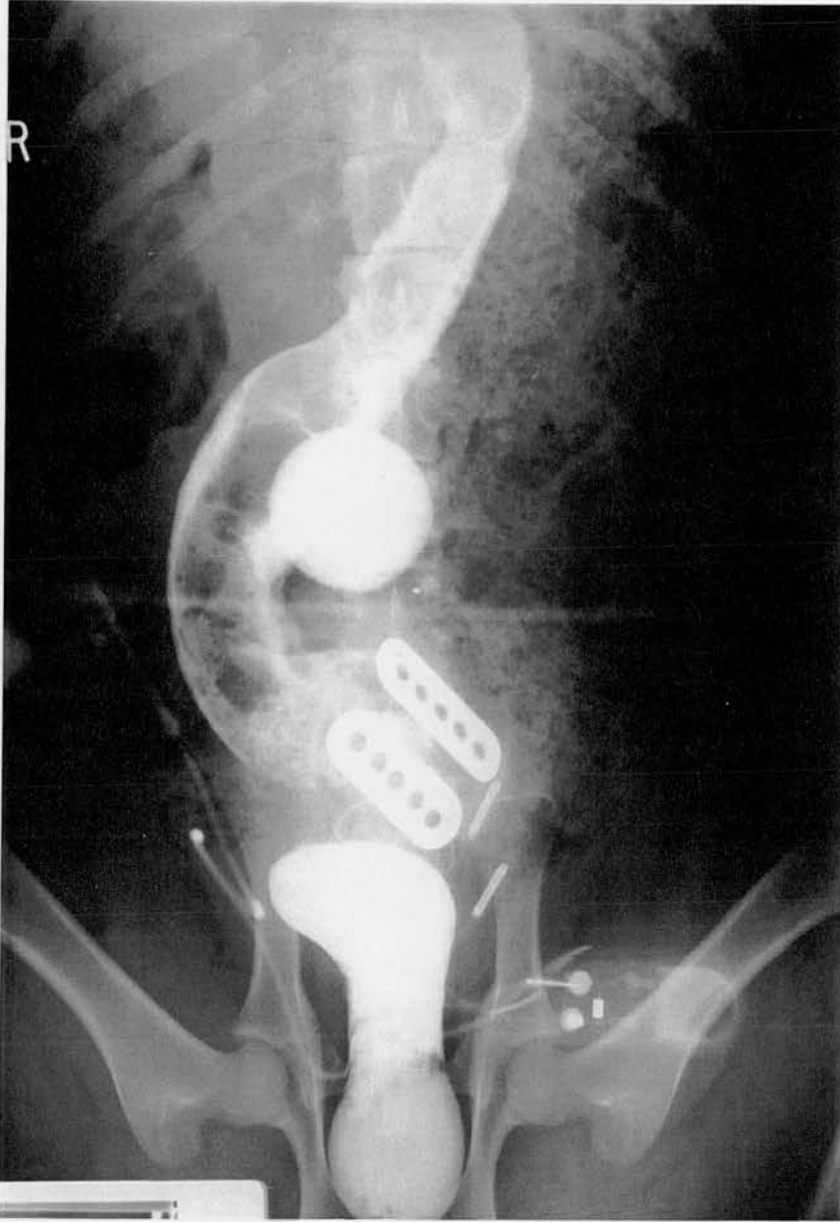


Figure 10: Ventrordorsal view with the distal bowel outlined with contrast. The rectum is seen to span the whole length of the center of abdomen to the splenic area. More proximally, it becomes the spiral colon anatomically (not shown).

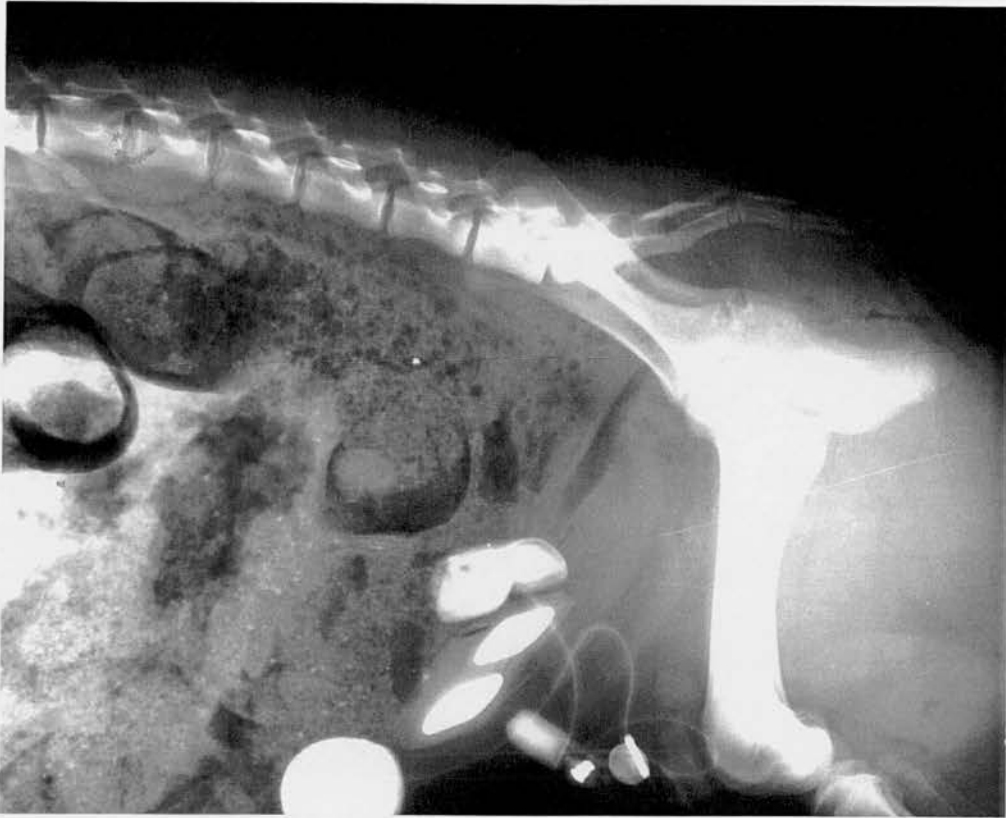


Figure 11: Radiological appearance of the AMS 800 pump which was implanted in one animal. As this pump does not have an injection port, a separate self sealing reservoir was implanted in order to provide access to the system percutaneously.

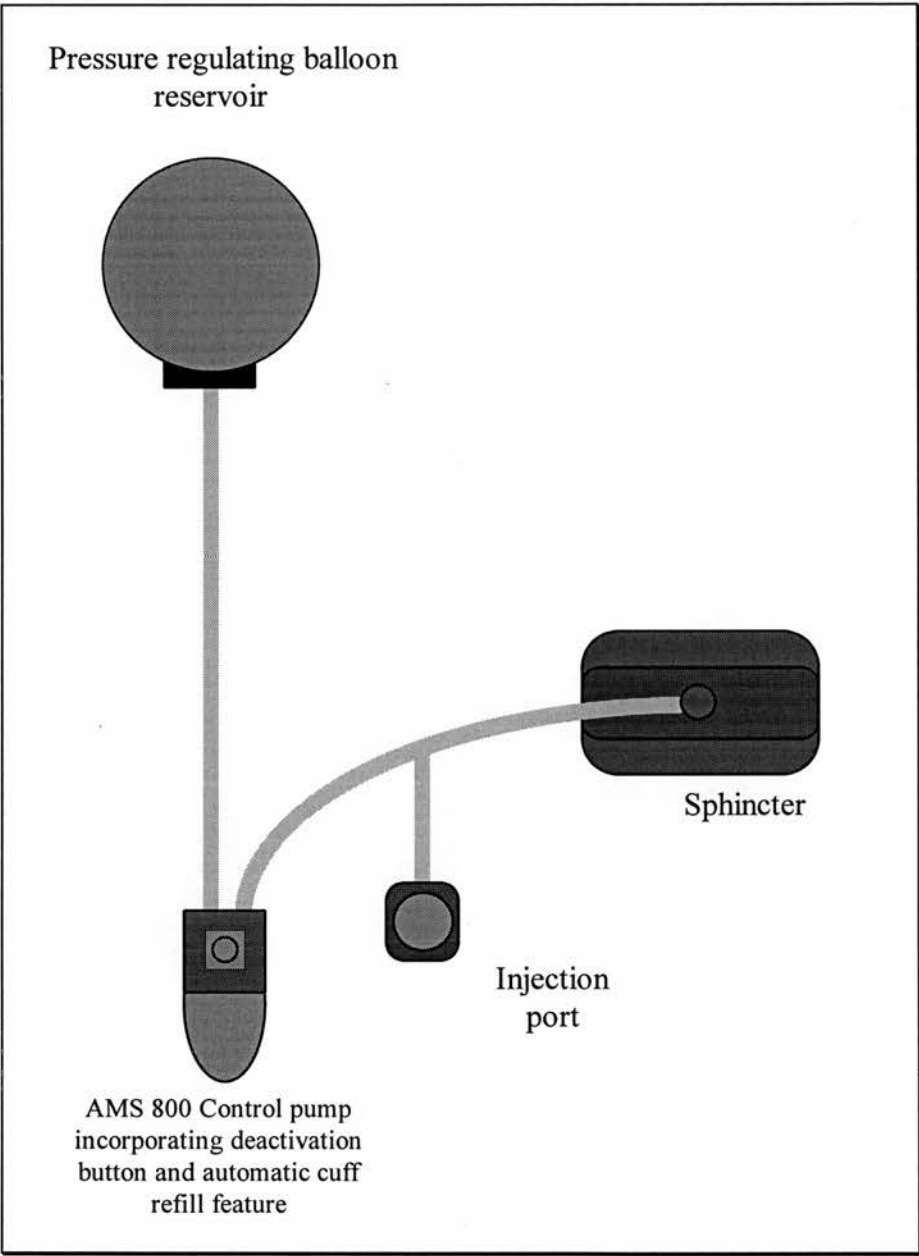


Figure 12: Diagrammatic representation of the implanted system incorporating the AMS 800 control pump and an injection port.

The hydraulic switch

Due to the unreliability of the shutoff valve and the resistor (Chapter 3, Chapter 6 and Appendix 5), one or two hydraulic switches were implanted with the system in an attempt to preempt and rectify the problems (Figure 13). However, the operation of the switch proved universally unsatisfactory. Following implantation, the air inside the gas permeable, flexible casing was reabsorbed and the casing collapsed and caused pressure on the switch itself (Chapter 3). This caused the switch to be maintained in a partially or fully closed position (Figure 14) and could not be operated manually. Contrast instillation into the casing via a 25 Gauge needle confirmed this by demonstrating waisting and kinking of the tubing (Figure 15). The appearance shown in Figure 15 is almost certainly worse in real life, as even the minutest volume of contrast injected into the casing, would relieve the vacuum and allow the switch to partially open. Further fluid injection into the casing relieved the vacuum and allowed the casing to re-expand thus allowing manual operation of the switch (Figure 16).

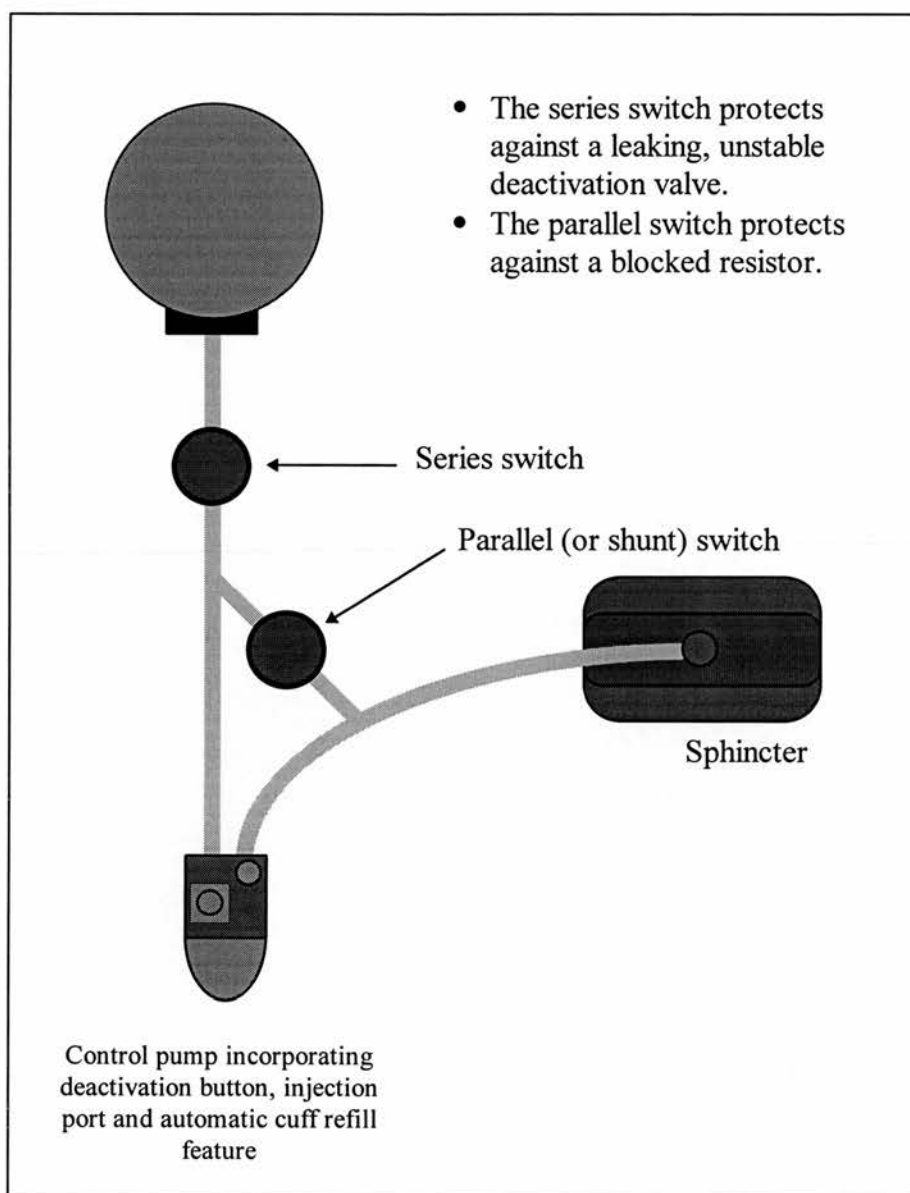


Figure 13: Diagrammatic representation of the implanted system incorporating the series and parallel switches.



Figure 14: Radiological appearance of the malfunctioning switch shown in close-up. Note the collapsed casing and the waisting of the tubing. This is caused by air reabsorption from the casing (see text).

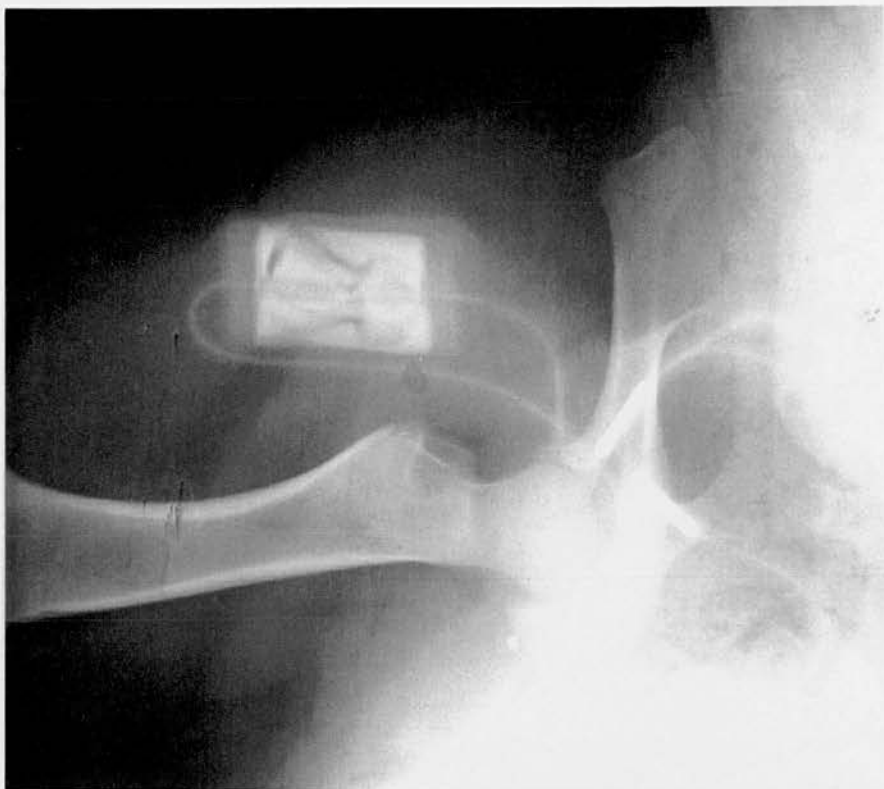


Figure 15: Close-up view of the hydraulic switch after contrast instillation into the casing. Waisting of the tubing is still present, even though the casing is partially expanded to its normal shape.

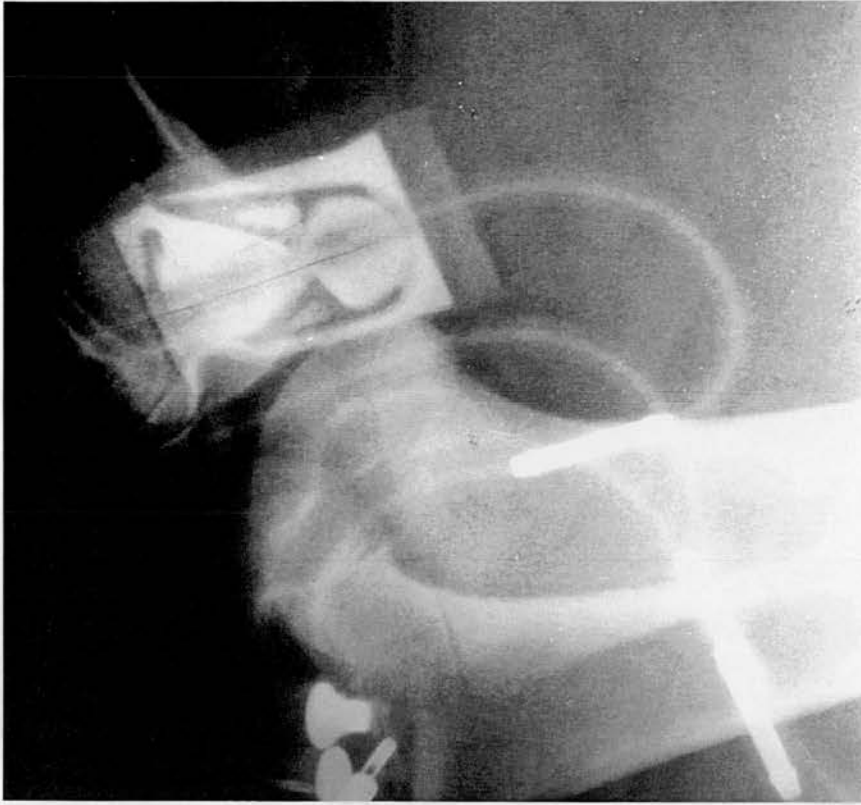


Figure 16: Further injection of fluid into the switch, relieved the vacuum and allowed manual operation.

System leakage

In one animal the system could not be inflated by routine puncture and fluid injection at the two week postoperative routine activation session. It was possible to inject fluid into the balloon, but this did not equilibrate with the expander (Figure 17). The pump could not create suction. There was radiological evidence of fluid leakage from the system (Figure 17, Figure 18). The contrast outlines the outside of the tube ("tramlining" in Figure 17) and the balloon surface (Figure 18), by leakage into and along presumed maturing fibrous tracts. This animal was therefore kept as an implanted control and terminated electively after 12.5 weeks. At routine postmortem the leakage was found to be from the pump casing.

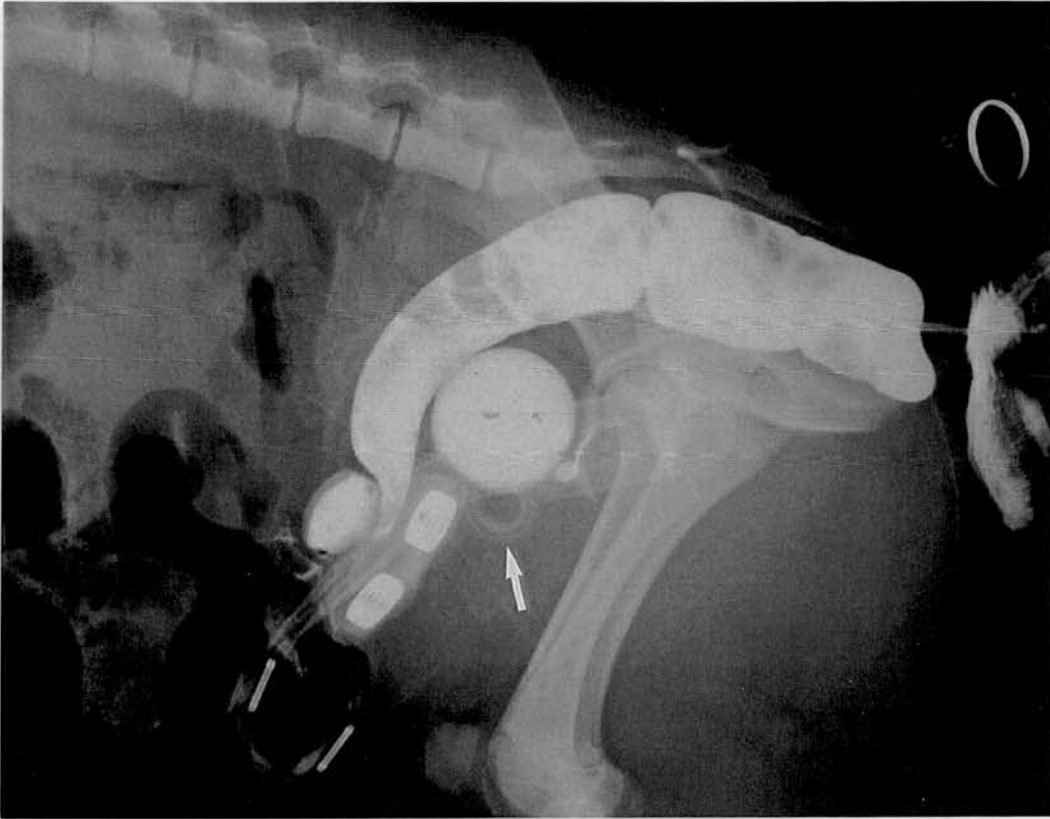


Figure 17: Contrast was injected in the system but leaked through the pump casing. It outlines the surface of the tubes and causes the “tramlining” sign: two radio-opaque lines separated by the radiolucent tubing (arrow).

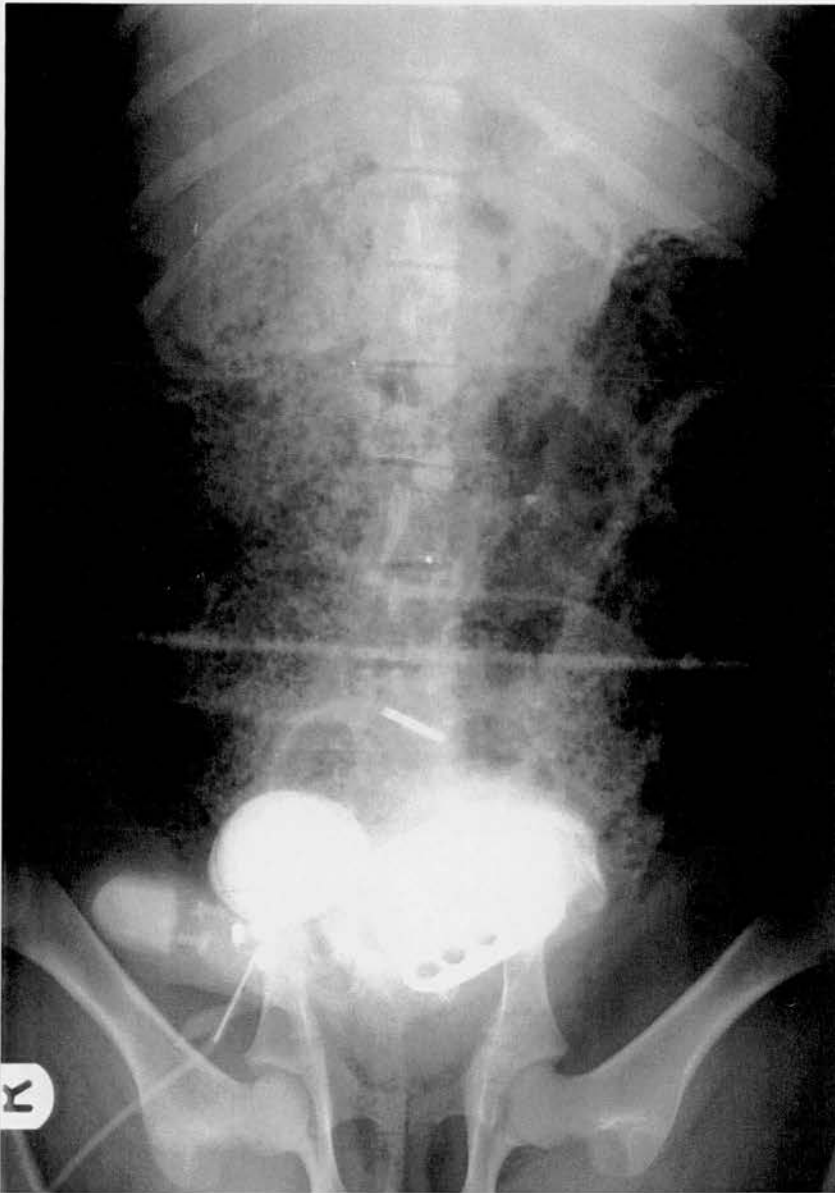


Figure 18: Crescent of contrast on the outside of the balloon of the animal discussed above (intervening dark line represents the thickness of the radiolucent balloon).

Colonic obstruction:

There were several episodes of colonic obstruction due to inadvertent activation of the control pump. This was always diagnosed clinically by palpation of the pump and resolved upon subsequent deactivation of the device. There were three episodes of colonic obstruction the cause of which was diagnosed radiologically: two were due to the impaction of hard stools and the third due to displacement of the expander in relation to the pillow (Figures 19 to 21).

One animal became constipated for two days. Fæcal loading was confirmed by plain abdominal X-Ray. A Foley catheter was passed per-rectum and a soapy water enema administered proximal to the neosphincter (Figure 19). There was good return of fæces and the obstruction was relieved. No other similar problems occurred in this animal.



Figure 19: One animal became loaded with fæces and received an enema. A Foley catheter was passed proximal to the sphincter to administer the enema with a good result.

Another animal suffered obstruction because of ingestion of the sawdust that was used to line the pen. This was also relieved successfully with an enema. Note the crescentic appearance of the empty expander at plain X-Ray (Figure 20). This was presumably due to stretching of the lumen at that point by the hard stool.



Figure 20: Lateral abdominal X-Ray of an animal with intestinal obstruction due to sawdust ingestion. Note the crescentic shape of the empty expander which is presumably due to stretching by the hard stool.

The last animal suffered obstruction because the expander element slipped in relation to the pillow (Figure 21). The bowel angulation was exaggerated and, in addition, the expander must have physically obstructed the flow of faecal material. For this reason, this animal was terminated prematurely.

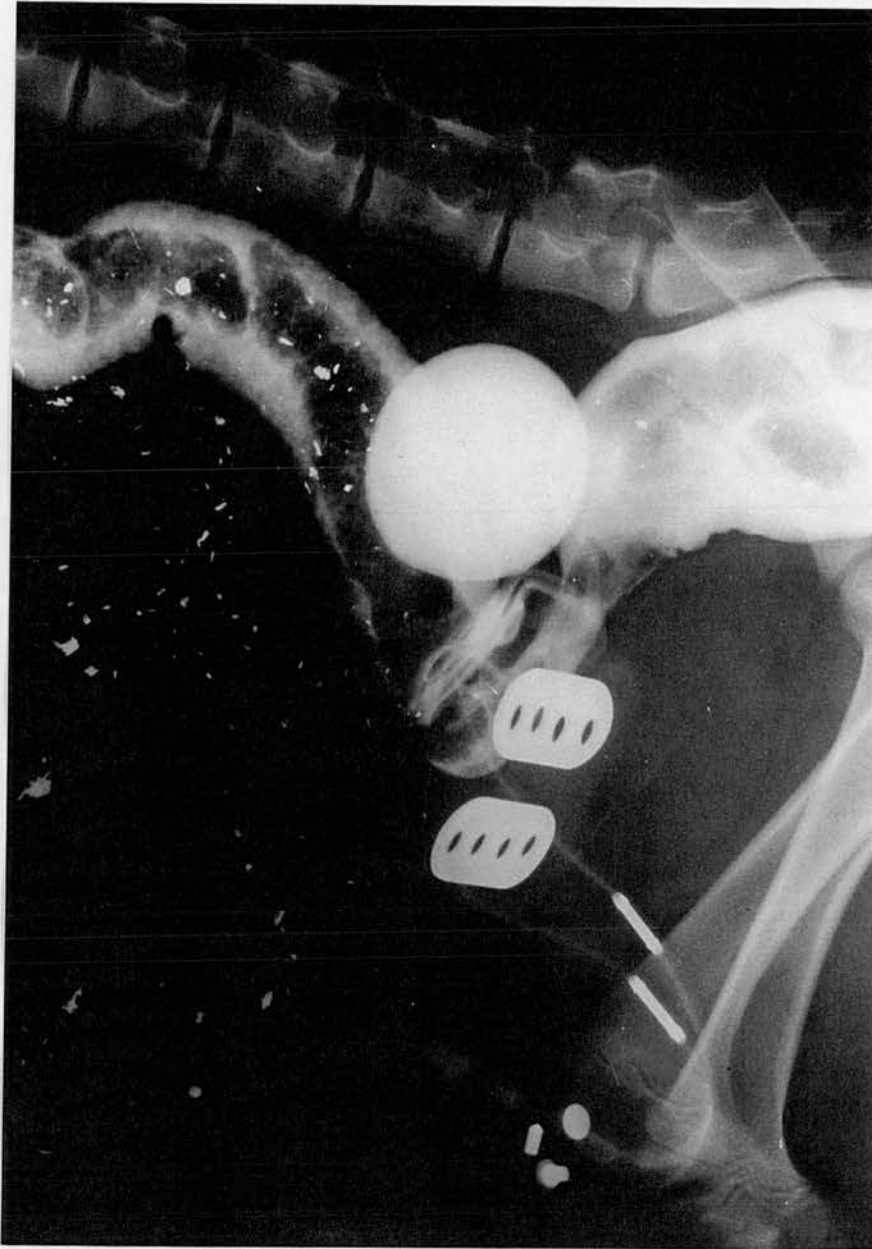


Figure 21: Colonic obstruction due to displacement of the expander in relation to the pillow.

Overall 25 plain radiographs and 24 contrast enemas were performed in 15 animals. The different types of investigations performed in the animals are summarized in Table 1.

ID.	Routine		Assessment for Complication		Malfunction	
	AXR	Contrast	AXR	Contrast	Component	Action/Other
#1	1	1				
#2	1	1				
#4	1	1	1	1	Slow resistor	Nil
#5	1	1			Pump leak	Control animal
#6	1	1	1	1	Switch activated	Injection into casing
#7	1	1	1	1	Expander straps loose	Replace Vicryl with Prolene
#8	1	1				
#11	1	1				
#12	1	1				
#13	1	1	1	1	Resistor blocked	Nil
#14			1			Constipation. Enema
#15	1	1	1	1	-Resistor blocked	-Nil
					-Switch activated	-Inject in casing
#16	3	3	2	2	-Resistor slow	-Multiple
					-Switch act. x2	(x1 deactivation / activation to perform transit
					-S/off Valve fault	

ID.	Routine		Assessment for Complication		Malfunction	
	AXR	Contrast	AXR	Contrast	Component	Action/Other
						studies)
#19	2	2				Pump replaced
#20	1	1				
Total: 17 17 8 7 = 25 plain, 24 contrast X-Rays.						

Table 1: Summary of radiological investigations.

A stepwise method for radiological assessment of this device based on our above experience is presented Figure 22.

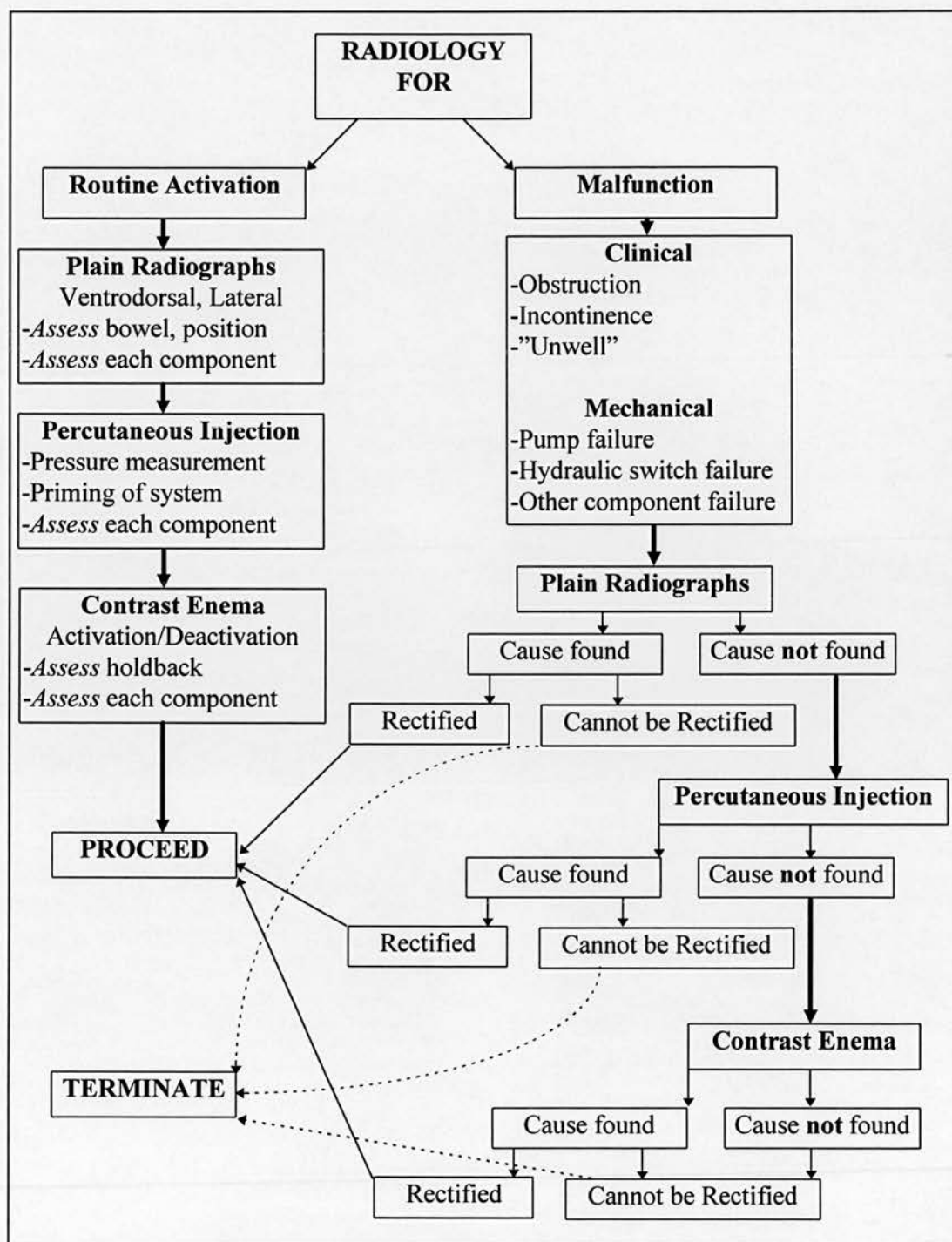


Figure 22: Radiological evaluation algorithm for the artificial anal sphincter prosthesis.

Discussion

Radiographic evaluation of this device postoperatively reveals functional adequacy (or inadequacy) of the prosthesis and aids in delineating malfunction aetiology. As the mechanical control and operation of this device is similar to that of the AMS urinary sphincter, the complications and method of assessment described above will be compared to those reported in the literature for the AMS device.

Pagani et al.² present the first series of radiological assessment of the early AMS models (AMS 742A/B/C). The guidelines on preoperative patient assessment and preparation they report are not relevant to this anal sphincter. Tubing kink and fluid leak from the system were the main complications they reported and this was confirmed by subsequent studies involving the AMS 792 model^{3,4} but not for the AMS 800^{4,6}. We did not encounter any complications pertaining to kinked tubing and this may be a reflection that, as with the AMS 800, kink resistant tubing was used.

We observed that fluid loss from the system was due to leakage from the pump casing due to a perforation. It was also shown that the self sealing mechanism incorporated in the pump was unsatisfactory. Gradual leak (or “bleeding”) from silicone prostheses is well established and fluid loss from the AMS system is known to occur gradually due to osmosis or contrast crystallization⁴. This complication was not definitely established by our observations as the time of follow-up of the experimental animals was much shorter than the patient series in which it was reported. In addition, leakage from the injection port would always overshadow the much slower leakage that occurs via osmosis across the silicone wall of the prosthesis.

Intestinal obstruction was mainly due to pump malfunction (inadvertent activation due to shutoff valve unreliability), which was usually diagnosed and dealt with clinically (Chapter 3, Chapter 6, Appendix 5). There were, however, three cases of colonic obstruction in which the diagnosis was made radiologically: one was due to constipation, the other due to sawdust impaction and the third due to displacement

of the cuff. The first two were treated by the administration of an enema under the same anaesthetic, but the latter animal had to be terminated as the only other way this could have been relieved would have been by revisional surgery as this was not allowed by the experimental protocol for reasons of animal welfare. Obstructive complications were also reported with the urinary device^{3,4}, both as causes of acute retention^{3,4} and chronic bladder outlet obstruction³ and were also reported by patients with a modified version as an anal sphincter^{9,10}.

In our experimental animal series, most complications that were analysed radiologically related to the pump (see Chapter 3 and Chapter 6) or its ancillary components (hydraulic switch). The thin silicone wall of the device allowed diffusion of air into the tissues, eventually creating a vacuum which exerted a collapsing force on the switch, causing it to close and become unusable. This occurred relatively quickly (within two weeks). It was readily diagnosed radiologically and treated, in the short term, by injecting approximately 1-2 ml of contrast into the casing to neutralize the vacuum. This, however, did not confer a long term solution as the fluid leaked out through the thin wall of the silicone casing by diffusion and the problem recurred almost as fast as it developed in the first instance.

Another complication encountered was inability to activate the pump following activation of the shutoff valve. This operation depends on a critical volume of fluid remaining inside the bulb prior to deactivation which will allow the subsequent generation of a surge of pressure by pressing on the bulb, thus unseating the shutoff valve. It was necessary to inject fluid into the bulb on several occasions to achieve activation and this was done during the general anaesthetic/radiology sessions. Other experimental parameters (bowel angulation, distance between the prosthesis and anal canal, bowel distention and anal tone/pullthrough pressure) were also evaluated during these sessions.

In one study where the modified AMS 800 device was used as an anal sphincter⁹, it is suggested that its effectiveness may be contributed towards by the maintenance of an acute anorectal angle.

The method of assessment of this device that has been presented does not involve any new techniques or equipment. The radiographic examination is the prime postoperative means of evaluating these prostheses as clinical feedback may be difficult to interpret or impossible to collect and endoscopic instrumentation may damage the rectum.

This new experimental Neosphincter may be implanted in humans as part of a pilot study, once the shortfalls that have been identified in the design and its construction have been corrected. This analysis would enable the professionals who have gained an understanding of the normal operation of the sphincter and its problems to effectively care for the patient who may be implanted with such a device in the future.

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Section 3

Human Implantation

Chapter 8

The effect of the Neosphincter on colonic blood flow distribution in Humans

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Summary

A laser doppler flow scanner prototype was used to assess the blood flow distribution in human colon intraoperatively in control patients and in patients with inflammatory bowel disease. The biological zero flow value was found to be 46 relative perfusion units. Blood flow was significantly higher in inflamed colon (332.8 PUs *versus* 286.4 PUs). The scanner demonstrated intestinal mural blood perfusion and was able to define ischaemia demarcation lines prior to visible changes ensuing.

The effects of progressive compression by the AASP 2000 artificial anal Neosphincter were also studied in the two groups of patients. Progressive reduction of blood flow was observed with increasing inflation pressures. Colonic blood flow remained above 48% of its baseline value even at levels of system pressure beyond the sphincters' planned maximum settings. It appears that the Neosphincter is not likely to cause ischaemic injury to the human colon at the planned occlusion pressures.

Introduction

Laser doppler flowmetry is a non-invasive technique which can be used to assess tissue blood flow¹⁻³. The method for extracting blood flow information from doppler spectra has previously been well demonstrated and the working principle of this method has been described in detail⁴⁻⁷. Blood flow is inferred by measuring the doppler frequency shift in light reflected from moving red blood cells in the tissue being studied. However, the static contact probe used so far has disadvantages which make measurements tedious and sometimes unreliable⁸. The probe must abut onto the tissue being studied and this influences the local blood flow⁹. Blood flow can only be measured in an area of approximately 3 mm², i.e. the detection area of a single light fiber source and detector. The technique is also susceptible to movement artefact and the results depend on the orientation of the fiber⁹.

A new technique has been presented¹⁰, whereby a laser beam remotely scans the biological area of interest (up to 0.5m²). This laser doppler flow scanner (LDS) directs a laser beam on to the surface of the tissue by means of a motor and mirror assembly. The reflected light contains doppler frequency and reflected light intensity information from which blood flow can be calculated. The beam is moved along the colon in a raster fashion and blood flow information from the reflected and doppler-shifted light is continuously recorded and stored in a computer. A colour coded image is constructed which shows the distribution of blood flow, expressed in arbitrary perfusion units (PUs). This data can be presented as a two-dimensional contour map, showing the blood flow distribution in the tissue of interest (Figure 1, Figure 2).

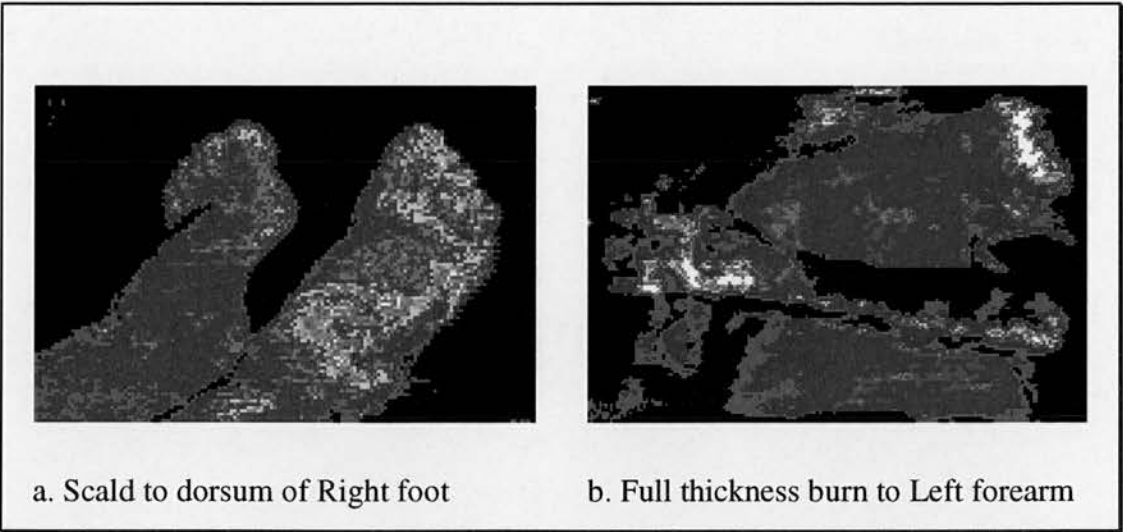


Figure 1: The laser doppler flow scanner was used to demonstrate increase blood flow and its distribution in partial thickness scald (a.) and no blood flow in full thickness burn (b.).

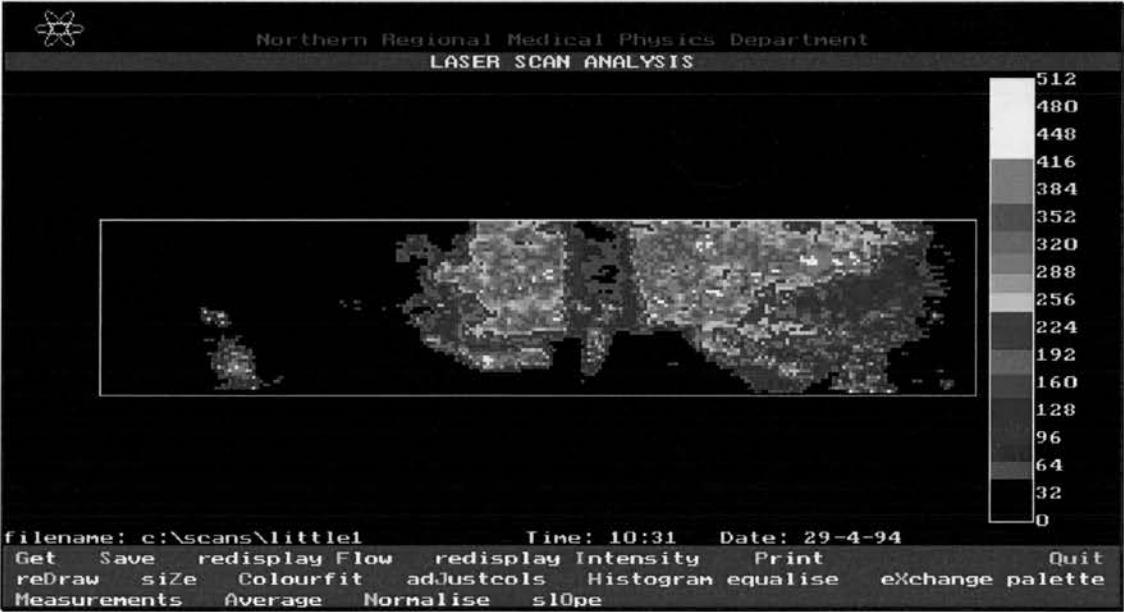


Figure 2: Sample trace of a scan of human colon blood supply distribution. Colour coded bar numbers represent arbitrary Perfusion Units (PUs). The Neosphincter is opaque to Laser light.

We have used the prototype laser doppler scanner (LDS) to measure and compare colonic blood flow distribution in 12 human volunteers undergoing colectomy (6 controls, 6 with inflammatory bowel disease). The effects of progressive compression by the AASP 2000 Neosphincter on colonic blood flow distribution were also compared in the two patient groups.

Patients and Methods

One patient was studied as part of a pilot study to assess the suitability of the static probe laser doppler flow meter (PeriFlux PF2; for method of static laser doppler measurements see Chapter 4). The setting of the Neosphincter was as described below. The blood flow measurements were cumbersome mainly due to movement artefacts and the extra anaesthesia time could not be justified both in clinical and service terms. The baseline readings were also quite variable (Appendix 4). For these reasons this technique was not used again and a further set of patients was assessed with the prototype flow scanner.

Twelve adult patients (eight males, four females, median age 49.8 years, range 24.3-78.7 - Table 1) were enrolled in the study. Routine bowel preparation with Picolax and Klean-prep solution was instigated pre-operatively. Six patients had colectomy for inflammatory bowel disease (I.B.D.) and six had colectomy for non-inflammatory conditions (rectal prolapse, carcinoma) and acted as controls. Routine biochemical and haematological investigations were obtained within 48 hours pre-operatively and on the first post-operative day.

	Age	Sex	Diagnosis		Age	Sex	Diagnosis
1	71	F	Rectal prolapse	7	40.23	M	U.C.
2	70	F	Crohn's disease	8	75.2	F	Carcinoma
3	78.7	M	Carcinoma, U.C.	9	30	M	U.C.
4	74.5	M	Carcinoma	10	31.8	M	Carcinoma
5	72.3	M	Carcinoma	11	24.3	M	Crohn's disease
6	46.4	F	Carcinoma	12	49.8	M	I.B.D.

Table 1: Details of the 12 patients studied with the laser doppler flow scanner.

One patient had colectomy for carcinoma following long term ulcerative colitis (U.C.) and was included in the inflammatory bowel disease group; another had inflammatory bowel disease of indeterminate histological type (Table 1).

Another patient (Id. No 2) was also diabetic and one patient had previous surgery (Id. No 5) and the only blood supply available to support the right colon was the ileocaecal artery. These two patients were excluded from the numerical analysis of the blood flow data.

Anæsthesia was induced with thiopentone and maintained with a nitrous oxide / oxygen / isoflurane mixture. Intra-operative cardio-respiratory parameters were continuously monitored. After mid-line laparotomy the colon was routinely mobilized and delivered through the wound. A segment of colon approximately 25 cm long was prepared for the experiments in the following way: the colon and its blood supply were stapled and divided distally and the dissection in the mesentery was continued until all the accessory feeding vessels were divided so that all blood supply came from a proximal feeding vessel (end-artery). The AASP 2000 Neosphincter was then placed around the bowel so that it encircled the whole circumference of the bowel including the end-artery (Figure 3). Upon inflation of the Neosphincter, the blood supply to the colon under the expander would decrease and this decrease would be reflected on the blood flow in the distal segment of the bowel which could be scanned. In two patients the bowel was not divided distally but was left in continuity having divided the distal blood supply (Figure 4) in order to demonstrate mural blood flow (a bowel clamp could be applied to the distal colon to mimic the conditions in the other 10 patients).

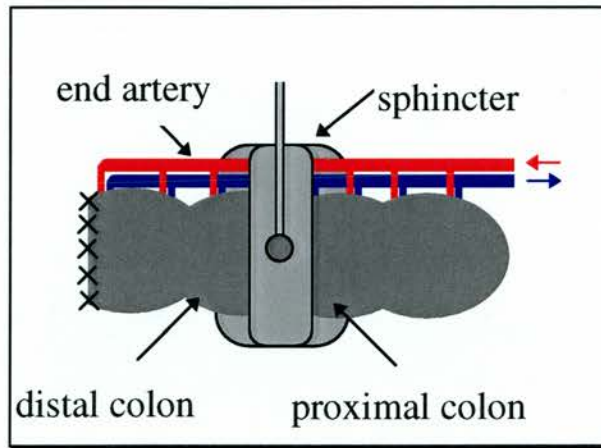


Figure 3: Experimental arrangement to study the blood supply distribution in the colon. The distal colon depends on its blood supply on the end artery which passes under the Neosphincter. Blood flow changes under the device should be reflected on the distal segment of the colon which can be scanned.

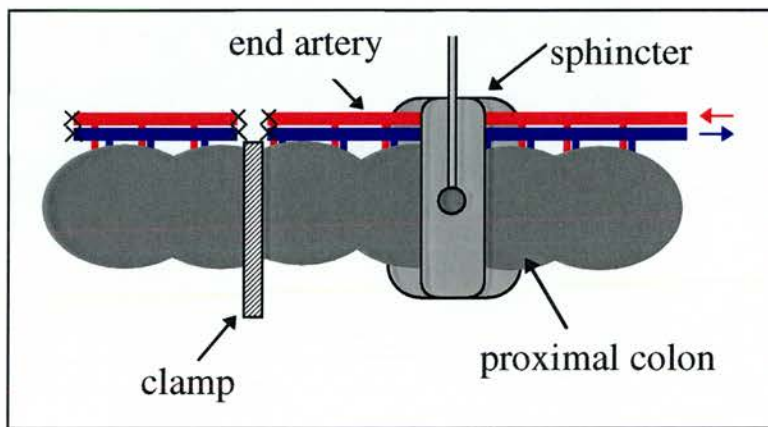


Figure 4: Experimental arrangement to study the presence of mural blood supply in the colon. Upon release of the clamp, any blood flow in the distal segment of the bowel could only be due to mural perfusion.

The straps of the expander were adjusted using the 22.5 mm specially designed sizer which was identical to that used in the animal experiments (Chapter 6). The expander was then inflated with normal saline to achieve inflation pressures of 30, 60 and 90 mmHg. The pressure applied by the sphincter on the bowel was measured at each stage by the station pull-through technique using a Gaeltec CTU1 catheter tipped microtransducer. All measurements were repeated three times. Both

the sphincter inflation pressure and pull-through pressure were continuously recorded on a Gould two channel Chart Recorder (Model 8188-2202-09, Gould Ltd, 57, Rue St. Sauveur, Ballainvillers, France).

Prior to using the LDS, the bowel was surrounded with operative theater drapes and all nearby metal objects were covered, in accordance with local safety protocols. The scanner was placed approximately 1m above the patient and the blood flow measurement performed without any contact with the patient or the sterile operative field. Standard lighting conditions were maintained throughout the measurements in all patients to prevent interference from bright ambient light sources. The surface of the bowel was scanned using the LDS with the sphincter uninflated, at each pressure setting and with the mesentery clamped in order to establish a biological zero flow reading. At the same time the, intensity of reflected light was measured and stored along with the doppler signal. These could be analyzed separately. Each scan took approximately 1.5 minutes. The artificial sphincter is opaque to laser light and can be easily identified on the scanned images (Figure 2, Figure 5, Figure 6, Figure 8). Image processing software¹⁰ was used to analyze selected areas of the colon proximal and distal to the sphincter on each scan. Each area contained several hundred reading points (pixels) and the average flow reading in perfusion units (PUs) for each area was calculated.

Statistical analysis

The unpaired t-test was used to compare the data.

Safety considerations:

Safety guidelines for the use of the laser doppler flow scanner prototype were drawn by the Department of Clinical Physics and Bioengineering, Royal Infirmary, Glasgow. The following discussion outlines the relative risk of retinal exposure to laser light and compares the static laser probe with the scanner.

Definition of terms:

Mean permitted energy on the retina (MPE):

$$\text{MPE} = 18 \times t^{0.75} \text{ Jm}^{-2} \quad \text{where} \quad t: \text{time of exposure}$$

Radiant energy received by the eye averaged over the area of limiting aperture (H):

$$H = (\text{Energy of laser} \times t_{\text{exp}}) / A_p$$

where $t_{\text{exp}} = \text{pupil diameter} / \text{scanner beam speed}$

and A_p : area of pupil

Also, laser power = 2 mW

Pupil diameter = 7 mm

Case 1: fixed beam

For an exposure time of 0.25 s,

$$\text{MPE} = 6.4 \text{ Jm}^{-2} \quad H = 13 \text{ Jm}^{-2}$$

i.e. protective glasses of transmission factor < 50% would be required.

Case 2: scanning beam

100 line scan takes 2½ minutes, \therefore 1 line takes approx. 1.5 s.

At recommended laser distance of 1 m, scan width is 35 cm

$$\therefore \text{beam speed} = 0.23 \text{ ms}^{-1} \text{ and } t_{\text{exp}} = 0.03 \text{ s}$$

$$\text{MPE}_{\text{Scan}} = 1.3 \text{ Jm}^{-2} \quad H_{\text{Scan}} = 1.6 \text{ Jm}^{-2}$$

i.e. protective glasses of transmission factor < 80% would be required.

Results

The pre-operative hæmoglobin (Hb), hæmatocrit (Hct) and mean corpuscular volume (MCV) were within the normal range and there was no significant difference in these parameters post-operatively (Table 2). The scans were stored by a dedicated computer and analyzed subsequently using specially designed software (Figure 2, Figure 5). The blood flow was averaged over a selected area of the bowel proximal and distal to the Neosphincter.

	Pre-op (S.D.)	Post-op (S.D.)	p
Hb	11.9 (2.14)	11.5 (1.78)	0.40
Hct	0.37 (0.06)	0.35 (0.05)	0.14
MCV	81.1 (7.42)	81.3 (7.02)	0.61

Table 2: Pre- and post-operative levels of hæmatological parameters that are known to affect blood rheological characteristics.

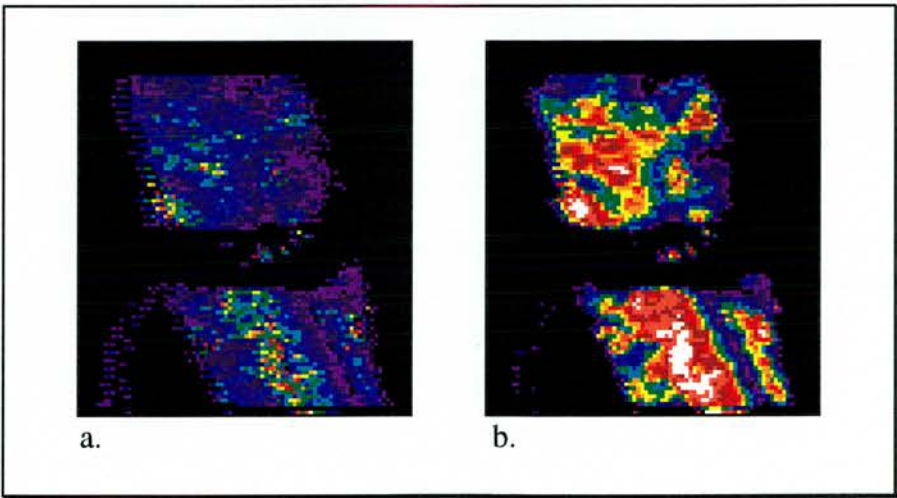


Figure 5: Laser Blood flow distribution scan before (a.) and after (b.) image analysis and enhancement.

In one patient the intensity scan showed that the colon was losing its reflectance during mobilization (Figure 6a) and ischæmia was confirmed by the doppler measurements (Figure 6b). A new demarcation/resection line had to be adopted as suggested by the doppler scan.

Figure 7 demonstrates the existence of intestinal mural blood supply. The distal segment of the colon is rendered ischæmic by the application of mesenteric and intestinal cross clamps (Figure 7a). Upon release of the intestinal clamp, the distal segment of the colon is perfused with blood from the wall of the proximal segment up to a distance of at least 6 cm.

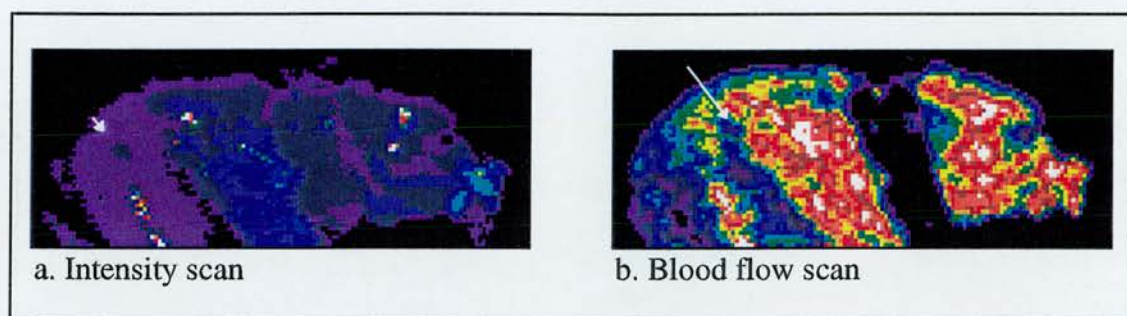


Figure 6: Demonstration of devitalized bowel during mobilization. Intensity data from the scan shows that bowel has lost its reflectance (a., arrowhead). Doppler scan clearly showed the perfusion demarcation line (b., arrow).

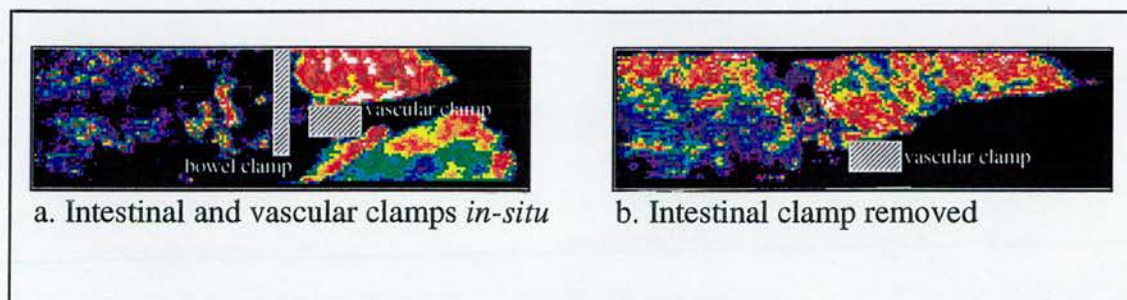


Figure 7: Demonstration of mural blood supply. The distal bowel is ischæmic after cross clamping its wall and the mesentery (a.). Upon release of the bowel clamp the distal segment is perfused through the wall of the proximal colonic segment (b.).

Scans were performed with the expander uninflated and inflated to 30, 60 and 90 mmHg. A specimen series of scans during progressive inflation of the Neosphincter is shown in Figure 8a-d. The operating occlusion pressures applied onto the bowel ($P_{\text{Pullthrough}}$) were approximately 0, 20, 38 and 58 mmHg respectively as the transmission factor was approximately 0.63 mmHg occlusion pressure per mmHg expander pressure (Figure 9).

There was no statistically significant differences in blood flow distribution in the colon proximal to the Neosphincter with progressive inflation of the device for each patient (Figure 10). The maximum decrease observed was from 275 PU (SD=11.5) at 0 mmHg to 200 PU (SD=42.1) at 67.5 mmHg (filled triangles, Figure 10). This occurred in a patient where only a small portion of proximal bowel could be brought into the scanning field. When the patient data was pooled together, however, a statistically significant decrease of 13% was obtained (from 317.6 PUs to 275.4 PUs, S.E.M.=50.1 and 51.7 respectively, $p<0.001$).

The “biological zero” value (i.e. the doppler flow reading with all blood supply clamped) was 46 PUs (S.E.M.=14.2) with no statistical difference between the two groups of patients ($p=0.88$).

Blood flow distal to the Neosphincter appeared to decrease progressively with increased sphincteric compression (Figure 9, Figure 11). When the raw flow values for all the patients were used, the correlation is poor ($r^2=0.14$). Even if the two patients with poor initial blood supply and diabetes are excluded the correlation is still weak ($r^2=0.25$). Stronger correlation ($r^2=0.48$) is observed when the blood flow is expressed as a percentage of the baseline value (Figure 12). In these circumstances, blood flow decreases by 0.34% per mmHg increase of expander pressure or 0.54% per mmHg increase of operating occlusion pressure (both patient groups pooled together).

The blood flow results in the two patient groups are compared in Figure 13 and Figure 14.

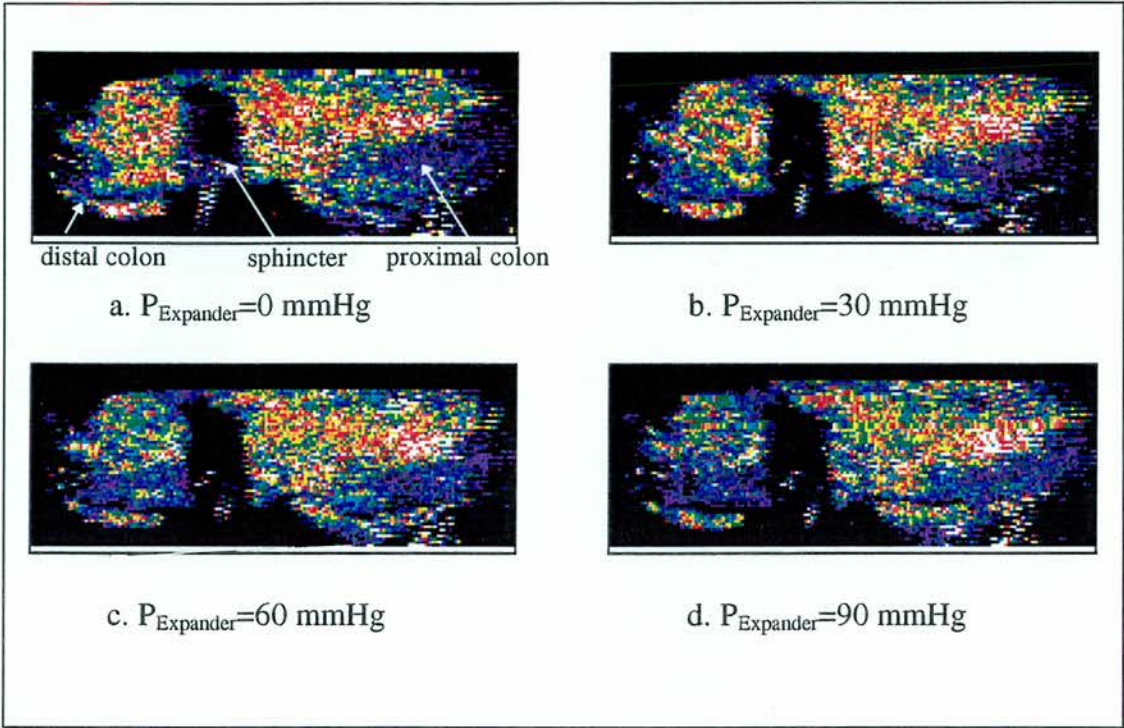


Figure 8: Specimen series of blood flow scans with progressive inflation of the Neosphincter.

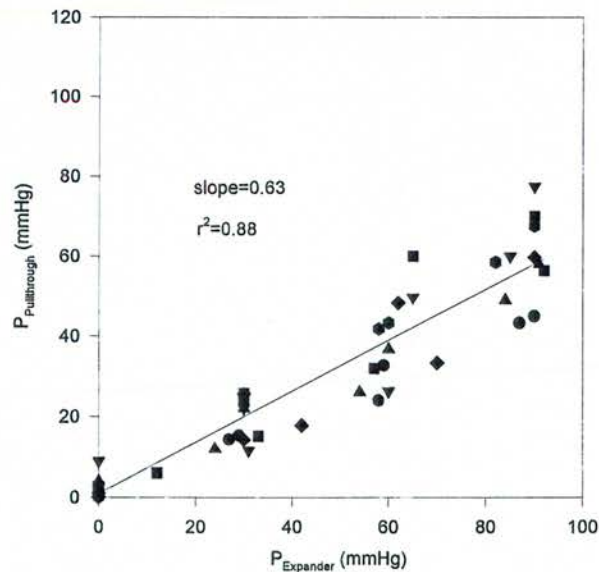


Figure 9: Correlation of operating occlusion pressure on the bowel ($P_{\text{Pullthrough}}$) versus expander inflation pressure (P_{Expander}) for the 12 patients.

The blood flow values were not statistically different in the colon proximal or distal to the deflated Neosphincter for the 10 patients as a whole group (322.5 PUs, S.E.M.=49.9 and 296.5 PUs, S.E.M.=35.5 respectively, $p=0.19$) or in the two groups separately ($p=0.24$ for control group and $p=0.34$ for I.B.D. group).

The blood flow in the whole segment of the colon (proximal and distal to the device) was significantly lower in the control group compared with the group with I.B.D. (286.4 PUs, S.E.M.=30.3 PUs and 332.8, S.E.M.=44.8 respectively, $p<0.01$). The blood flow in the different segments of the colon in the two groups without sphincteric compression is summarized in Table 3.

	Control (S.E.M.)	I.B.D. (S.E.M.)	P
Whole colon	286.4 (30.3)	332.8 (44.8)	<0.01
Proximal segment	297.8 (24.5)	347.2 (59)	0.12
Distal segment	274.7 (33.6)	318.3 (22.6)	<0.05

Table 3: Comparison of blood flow in the colon segments for the two groups of patients.

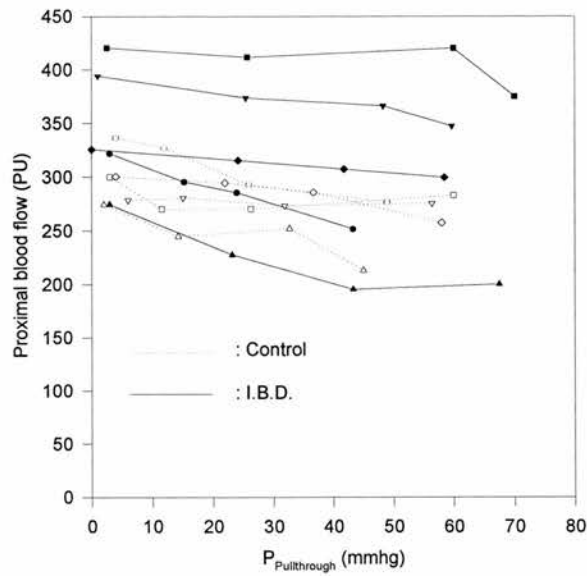


Figure 10: Blood flow distribution in the colon proximal to the Neosphincter *versus* progressive compression (both patient groups).

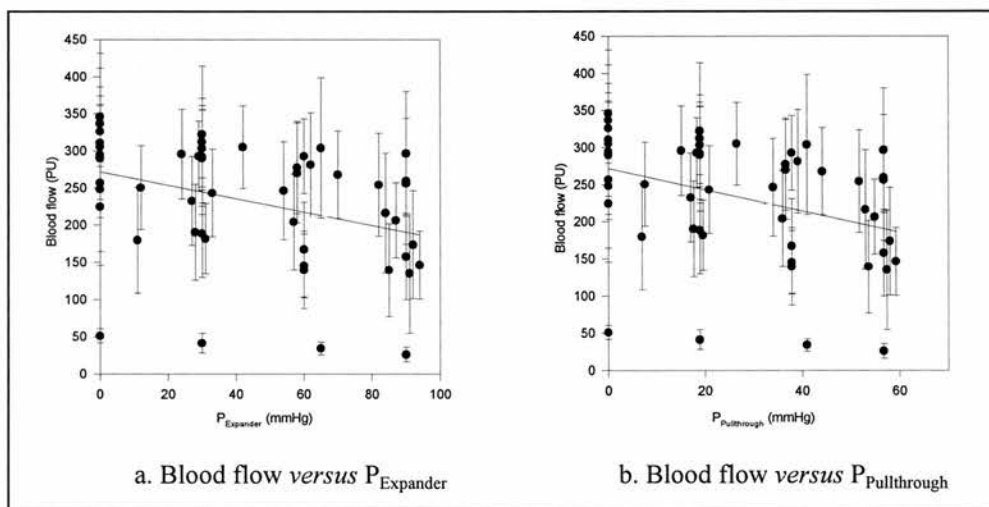


Figure 11: Blood flow distribution in the colon distal to the Neosphincter *versus* progressive compression (both patient groups).

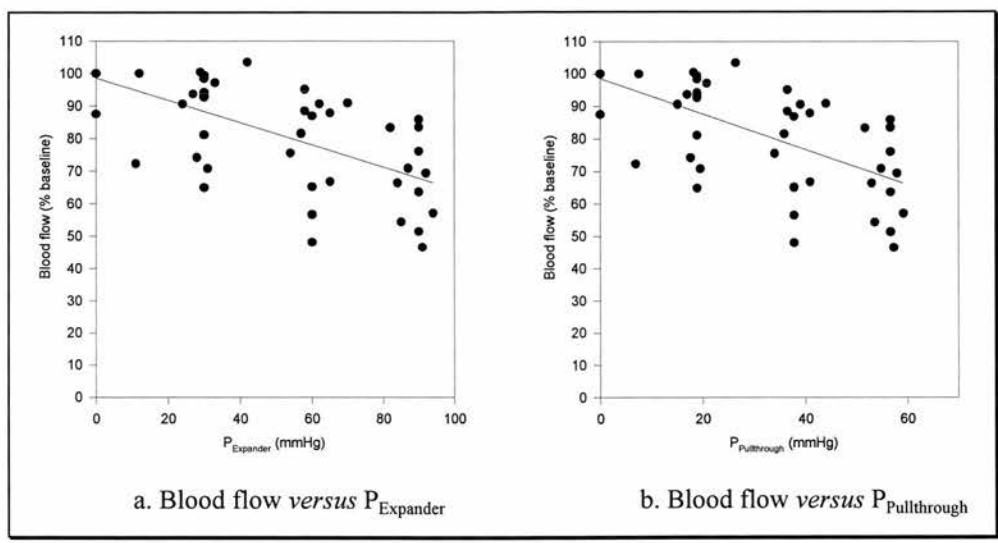


Figure 12: Blood flow distribution in the colon distal to the Neosphincter expressed as % of baseline *versus* progressive compression.

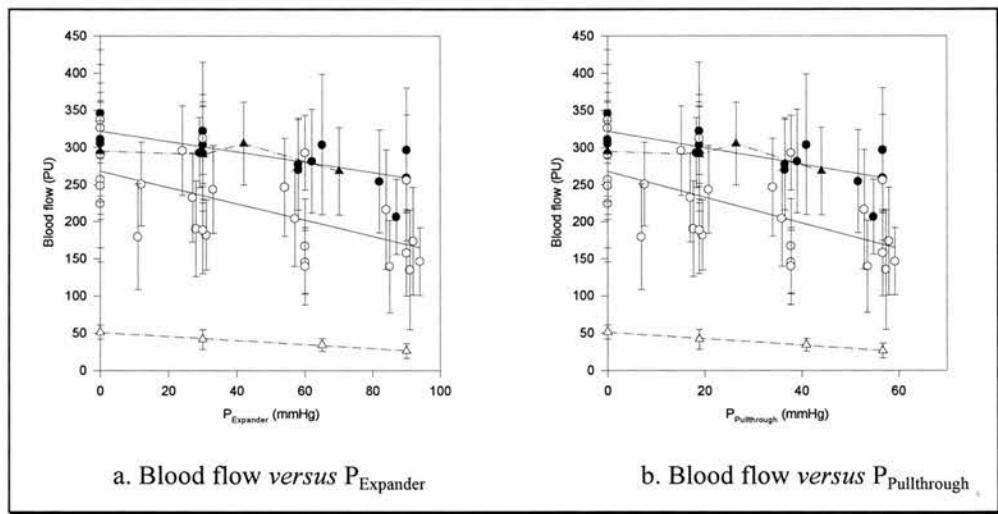


Figure 13: Blood flow distribution in the colon distal to the Neosphincter *versus* progressive compression. Comparison between patients with inflammatory bowel disease (filled symbols) and controls (open symbols). Data from the two excluded patients are also shown (legends as in Figure 14).

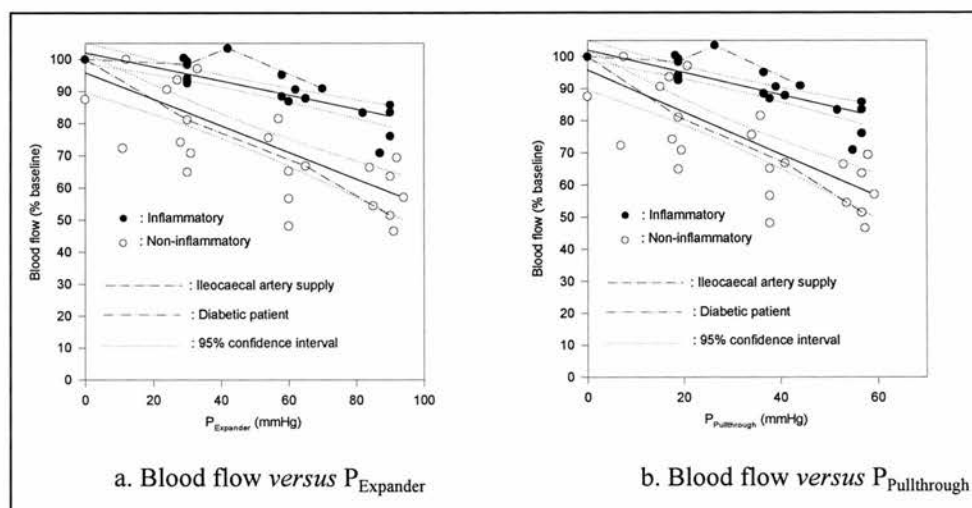


Figure 14: Blood flow distribution in the colon distal to the Neosphincter expressed as % of baseline *versus* progressive compression. Comparison between patients with inflammatory bowel disease and controls. Data from the two excluded patients are also shown.

The data plotted in Figure 13 and Figure 14 indicate that inflamed colon is less sensitive to the application of pressure. When the raw blood flow values are plotted (Figure 13), the correlation is weak (see Table 4) and the spurious data from the two excluded patients would further weaken the relationship. When the blood flow values are expressed as a percentage of the baseline value (Figure 14) the correlation becomes much stronger (Table 5). The blood flow changes in the patient with the ischaemic colon are now well within the confidence interval of the population and could be included in the analysis. The only spurious results are those of the diabetic patient with calcified vasculature.

	r^2	Blood flow decrease (PU per mmHg P_{Expander})	Blood flow decrease (PU per mmHg $P_{\text{Pullthrough}}$)
Controls	0.37	-1.09	-1.74
I.B.D.	0.56	-0.69	-1.1
Ischæmic	0.99	-0.27	-0.43
Diabetic	0.37	-0.33	-0.52

Table 4: Blood flow decrease in the two patient groups and the excluded patients.

	r^2	Blood flow decrease (% per mmHg P_{Expander})	Blood flow decrease (% per mmHg $P_{\text{Pullthrough}}$)
Controls	0.64	-0.41	-0.66
I.B.D.	0.72	-0.22	-0.35

Table 5: Blood flow decrease (% of baseline) in the two patient groups.

Discussion

A review of laser doppler flowmetry with special reference to the gastrointestinal tract:

Single fiber static laser doppler flowmetry has been used to assess gastrointestinal blood flow in animals^{9,11-29} and humans^{8,21,22,30-39}.

The results correlate well with tissue oxygen tension^{18,37} but are unaffected by hypoxia⁴⁰. Blood flow measurements in the gastro-intestinal tract also correlate well with isotope wash-out techniques (⁸⁵Kr washout¹⁵, Hydrogen clearance^{19,24,25,27,41}, ¹³³Xe washout in nasal mucosa⁴²), fluorescein flowmetry³⁶, radioactive microsphere distribution¹⁶ and electromagnetic flow probe measurements¹⁸.

There are three main limitations of the technique of single fiber laser doppler flowmetry:

1. Blood flow is measured in relative perfusion units and the geometry of the probe influences the flux measurements^{29,43}. The instrument, therefore, requires re-calibration each time a set of experiments is performed^{15,19}.
2. The measurements are made in a very small volume of tissue⁴⁴ (typically 1 mm²), therefore single readings are unrepresentative due to the variability in spatial distribution of blood flow in most tissues.
3. The fiberoptic laser-guide and detector fiber sensor is susceptible to movement artefact or changes in orientation²¹ and is required to exert pressure^{21,45} on the tissues to avoid optical dissociation²¹, thus affecting local blood flow²¹.

One way that some of these limitations and the inter-observer variations (12-35%) reported^{8,46} can be partially overcome is to take multiple readings over a relatively extended period of time^{29,46}. In addition, several probe designs have been developed.

A microprocessor controlled moving arm was developed in order to move the laser probe to precise coordinates⁴⁷. It does not, however, serve to solve the methodological problems of the technique. An integrating probe containing seven

separate detector units arranged circumferentially in one flat package has been designed⁴⁴. The blood flow value is averaged between the detectors. A standard probe was placed in the center of the device and the two compared both *in-vitro*⁴⁴ and *in-vivo*^{44,48}; significant correlation between the two was reported^{44,48}. A special hybrid probe which incorporates a Hydrogen electrode in order to self calibrate the instrument to absolute flow values has also been reported⁴¹. Perhaps a more useful approach is that whereby a very small semiconductor unit which incorporates both the laser emitter and detector is placed directly on the tissue⁴⁹. This is still a "contact measurement" method, however, which may perturb the local blood flow distribution.

At zero blood flow conditions (e.g. with the tissue vasculature clamped) there is a persistent laser flux reading⁵ or "biological zero" (BZ) value amounting to approximately 15% of the baseline flow value. This phenomenon may be due to Brownian motion of the red blood cells and small random movements of the tissues. Laser light of a different wavelength may contribute to a reduction of this artefact⁴⁸. This BZ value was relatively small in well perfused tissues (5-10% of baseline on a warm toe) but much larger in relatively ischaemic tissues⁵⁰ (59-83% on a cold malleolus).

There was an initial debate as to whether the blood flow measurements obtained by the laser doppler instrument represented part or the full thickness of the bowel wall. An early study suggested that the mucosal blood flow could be measured separately from that of the serosa¹⁴, a fact that has not been confirmed by subsequent studies in animals^{15,16,18,20,24} and humans^{20,30,31,34}.

In a theoretical analysis of the factors that affect sampling depth Jakobsson and Nilsson⁵¹ showed that thicker optical fibers had a deeper tissue penetration and this was also dependent on the bio-optical characteristics of the tissue studied. Their results also suggest that a single optical fiber (acting both as the laser emitter and detector) had a shallower penetration depth than a multiple fiber arrangement whereby one or more acted as the emitter and the other as the detector. Thicker optic

fibers more widely spaced achieved an increased depth of measurement at the expense of the linearity of measurements. These results were confirmed in an *in-vivo* animal study²⁹. Statistically, the larger probes (three fibers of diameter and center separation $>500\ \mu\text{m}$) with transmural colonic penetration offer more reproducible results in that reproducibility within $\pm 10\%$ can be achieved with three as opposed to ten measurements required for the finer probes²⁹.

The depth of penetration is approximately 1 mm in skin^{2,10} and 6 mm in human colon²⁰, probably representing a composite or an integral of the transmural blood supply^{20,43}.

Perhaps the most significant development in the field of laser doppler flowmetry was the introduction of the laser doppler flow scanner¹⁰. It has a spatial resolution of at least 3 mm and it offers a fast and reliable method to produce a blood flow distribution map of a biological tissue of interest. It is a no-contact method with obvious methodological and patient advantages (e.g. no compromise of sterility of operative fields).

Two further reports on similar instruments have been subsequently made^{52,53}. The prototype versions of both these instruments have been assessed *in-vitro* and also on human skin. A smaller scanning surface ($0.15\ \text{m}^2$) and shallower measurement depth (0.25 mm) have been reported⁵². The measurements correlate well with ^{133}Xe washout blood flow measurements⁵³.

In our experiments, an evolution prototype of the instrument reported by Essex and Byrne¹⁰ was assessed. This instrument was able to evaluate blood supply distribution and analyze it effectively. The statistical analysis functions incorporated in the software allowed averaging, histogram equalization and standard deviation measurements to be made on the raw data. There have been several studies to assess colonic blood flow using single fiber laser flowmetry in cats²⁰, dogs^{18,27,54} pigs^{46,55} and humans^{30,33,37,38,56,57}. This is the first report of the measurement of colonic blood flow distribution by the laser doppler flow scanner. The instrument can also be used

to assess various conditions (colostomy blood flow³³, effects of radiation⁵⁷ and safe levels of blood flow for the viability of colonic anastomosis⁵⁷) more thoroughly.

Colonic ischaemia was demonstrated both by the intensity and the doppler flux scans prior to visible changes ensuing (Figure 6). Upon completion of the operative dissection, visible ischaemic changes were obvious and the resection line was modified according to that previously indicated by the scanner. The time consuming studies on discrete point blood flow measurements on ischaemic intestine in animals^{11,23,24,27,28} and humans^{32,35} could be expanded by applying the scanning technique to large segments, even the total length, of the bowel.

We were also able to demonstrate the presence of mural blood supply along the large intestine to a distance greater than the width of the bowel wall (Figure 7).

The blood flow values were not statistically different in the colon proximal or distal to the uninflated Neosphincter for the 10 patients as a whole group or in the two groups separately. The blood flow in the whole segment of the colon (proximal and distal to the device) was significantly lower in the control group compared with the group with I.B.D. and this is in accordance with a previously reported study³⁷. The hyperaemia associated with I.B.D. is well recognized and, whereas demonstrating it endoscopically with the laser doppler fiber may represent an interesting research finding³⁷, the doppler scanner may be able to demonstrate segmental I.B.D. activity in the whole length of the intestine intraoperatively.

The model presented in this study attempts to circumvent the problem posed by the fact that the Neosphincter is opaque to laser light. Clearly it would be useful to obtain an estimate of the effects of the Neosphincter on blood flow to assess its safety for human long-term implantation. This model allows this estimate to be obtained because the blood supply of the bowel depends on an end artery which passes under the Neosphincter. Changes in blood flow under the device should be reflected in the distal segment of the colon which could be scanned. The expander inflation pressure can be directly correlated with the operating occlusion pressure as measured by the pullthrough method because this device applies pressure on the

bowel evenly, without causing crenation or localized areas of pressure gradients (see Chapter 3, Chapter 4).

Upon inflation of the Neosphincter there was a small but significant decrease in the blood flow measured in the colon proximal to the device (Figure 10). This may be related to part of the bowel being angled and obscured under the expanding sphincter. It may also be related to the fact that as the resistance to blood flow increases by the inflation of the expander, this causes a decrease in the total possible outflow past the device, thus also decreasing the inflow of blood to the colon.

Figure 9 shows that the setting of the sphincter around the bowel was consistent in all the patients studied. Even though there was such a good correlation between the expander pressure and the pull-through pressure, the latter more faithfully represents the actual intra-luminal pressure in the bowel. The same settings were also used in the survival animal experiments (Chapter 6).

The blood flow in the diabetic patient did not decrease significantly with increasing sphincteric compression (Figure 14). The presence of calcified arterial vasculature in diabetes of long standing is well recognized and this may explain the above finding. The presence of poorly compliant vasculature in inflammatory bowel disease may also explain the fact that inflamed bowel is less sensitive to the application of pressure (Figure 13, Figure 14). Even though the compliance of the vasculature in I.B.D. has not been measured to date, it is conceivable that the inflammatory infiltrate and fibrosis surrounding the blood vessels may contribute to the causation of this observed effect.

The BZ value of the laser doppler flow scanner (LDS) was similar in magnitude to that of the static instrument⁵. As this parameter is a significant proportion ($\approx 15\%$) of the resting laser doppler flux measurement, it was taken into account when reporting the decrease of the colonic blood flow as a response to sphincteric compression.

In non-inflamed bowel, inflation of the Neosphincter to 30, 60 and 90 mmHg caused progressive decrease of the blood flow to 75%, 63% and 57% of its baseline

value respectively. When the level of BZ is accounted for, the corrected levels of blood flow are 64%, 54% and 48.5% respectively. A balloon plateau pressure of 70 mmHg is planned for the human implantation study and this should produce an operating occlusion pressure of less than 45 mmHg. Blood flow should, therefore, not be decreased to less than 50% of its baseline value by the device.

It is generally accepted that the intestine can tolerate chronic reduction of its blood supply to approximately 50% of its baseline. Since blood supply of approximately 30% of baseline is sufficient to allow healing of colonic anastomoses²⁷ and on the basis of the previously reported *in-vitro* and animal results in this thesis, and also the fact that the AASP 2000 Neosphincter prototype does not reduce the blood flow in colon to below 48% of its baseline value even at levels of system pressure beyond its planned maximum settings, it appears that the Neosphincter is not likely to cause ischaemic injury to the human colon at the planned occlusion pressures.

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Chapter 9

Protocol for long term Human implantation

Design of Clinical Trial of AASP 2000 artificial anal sphincter prosthesis

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Local Ethics Committee approval obtained on 22nd April 1996.

Description and intended purpose of the device:

Prosthetic implantable anal sphincter intended to correct faecal incontinence. In summary, a new design of pump has been utilised, the tubing and connectors have been made 'kink free' and a new design of sphincter is employed whereby a linear pillow and expander are used to flatten the bowel rather than a circular cuff which might cause crenation.

Aims and objectives of clinical investigation:

Assessment of a prosthetic implantable anal sphincter in human subjects.

Design of study:

Based on the Helsinki convention

Number of patients involved: 12

Number of devices to be used: 12

Duration of study:

Two years intensive follow-up, followed permanently less intensively.

Proposed Start Date: 01/07/96

Proposed Completion Date: 01/10/98

Implantation Period: 3 months

Control group:

The use of a control group for this study is not appropriate.

Criteria for subject selection, inclusion, exclusion and withdrawal:***Selection:***

Subjects with severe faecal incontinence who have the manual dexterity and intelligence to use the pump, and whose only realistic alternative therapy is a permanent colostomy.

Inclusion:

Subjects shall be between 18 and 70 years, otherwise fit and healthy with no intercurrent disease.

Exclusion:

Subjects who cannot operate the device or are unfit for the operative procedure. There will be a preliminary instruction/consultation when the prospective subjects will have to demonstrate that they can use and understand the function of the device. If they fail this evaluation they will be excluded.

Withdrawal:

Subjects will be withdrawn at the discretion of the clinicians, if they have any serious complication, or at the patients' request.

Subjects requiring deactivation of the device will not necessarily be withdrawn from the investigation and will be followed up for the full duration. If required, components may be removed/explanted and replaced when the complications subside or are remedied. All such incidents shall be reported on case report forms.

Provisions for recovery of the device:

All explanted devices or components shall be returned to Biosil for investigation / testing.

Methods of follow up and assessment during the investigation:

Subjects will be managed routinely during the post-operative period. The devices shall remain in the deactivated state for a period of four weeks. The device will be activated under careful ward supervision and patients will remain in hospital until device operation is satisfactorily. Before being discharged, the subjects will be issued with clear instructions and be given a thorough assessment. This will include a 24 hour contact telephone number for use if any complications arise, to ensure that they are seen by physicians who are familiar with the prosthesis and aware of the procedures. Once the subjects are discharged from hospital they will be reviewed as described in Table 1. During these reviews, the functioning of the device will be measured using ano-rectal physiology studies and / or radiological assessments on approximately a monthly basis. After 3 months, the studies will reduce to every 3 months for a further 6 months. The approximate timings for the studies are marked on the table with "S". All observations and medication administered shall be recorded on the Case Report Form. This form shall also be used to record all adverse events and adverse device effects.

	Time elapsed since hospital discharge		Time elapsed since hospital discharge
1	1 week	9	6 months - S
2	3 weeks	10	8 months- S
3	1 month - S	11	10 months
4	6 weeks	12	1 year - S
5	2 months - S	13	1 year 3 months
6	10 weeks	14	1 year 6 months - S
7	3 months - S	15	1 year 9 months
8	4 months	16	2 years - S

Table 1: Approximate review schedule.

Description of procedures to record and report severe adverse events and adverse device effects:

The investigators shall record adverse events and adverse device effects in the subject's case report form. The investigators shall inform without undue delay Biosil about any severe adverse event and adverse device effect, and provisions made in writing or by telephone or fax with written confirmation. In any emergency situation the investigators shall exercise their judgement to safeguard the subject's interests. In that case deviations from the clinical investigation plan shall not require the prior approval of Biosil or the Ethics Committee. Such deviations shall not be considered as a breach of agreement and shall be reported to Biosil.

Biosil will keep records of any adverse events and adverse device effects reported to Biosil during the clinical investigation, as per the normal customer complaints procedure contained within the corrective and preventative action procedure. Biosil is responsible for informing in writing all clinical investigators about the severe adverse events and adverse device effects. This information will be transmitted within ten days. Biosil will consider jointly with the clinical investigators all adverse events and adverse device effects and if required Biosil shall report them to the appropriate authorities as per Biosil's medical device vigilance procedure contained within the advisory note and recall procedure. The investigators shall inform the Ethics Committee of any severe adverse device effect.

Description and justification of statistical design:

There is no need for statistical method and analysis as the study is an all or none, line study of 12 consecutive subjects.

The first patient is scheduled to be implanted on 21st August 1996.

Conclusions

The need for an Artificial Anal Sphincter for a selected group of patients has been established in the historical reviews in the introductory section.

The data presented in the first two chapters discount the importance of the anorectal flutter valve theory for faecal continence and suggest that liquids are retained in the rectum by anal occlusion pressure alone, whereas the retention of semi-solid material is enhanced by anorectal angulation. The faecal substitute specifically designed for these experiments may be clinically useful in dynamic anorectal imaging investigations (videoproctography, isotope proctography).

The newly developed AASP 2000 Neosphincter which was described in this thesis appears to be free from the ischaemic complications associated with circumferential occlusive pressure on the bowel. It achieves this by applying the occlusion pressure in an even way over a large area, without creating localised pressure points. The creation of angulation also allows for the operating occlusion pressure of the sphincter to be set at even lower levels (approximating the lower end of the normal range of resting anal pressure in humans) and this increases the safety margin of the device.

The study in the survival minipig model suggests that the neosphincter produces faecal continence without intestinal ischaemia. The presence of the deactivated neosphincter did not influence the colonic transit time in the minipig. At present, reliability of the Neosphincter is limited only by the performance of the pump.

The algorithm developed for the radiological assessment of the function and complications of the implanted device should be useful in humans.

The disadvantages and limitations of the static, single probe laser doppler blood flow meter have been largely overcome by the new laser doppler flow scanner

prototype which was used to assess blood flow in inflamed and non-inflamed colon in human volunteers.

Blood flow was significantly higher in inflamed colon. The scanner demonstrated segmental hyperaemia, and visually confirmed the existence of intestinal mural blood perfusion. The scanner was also able to define ischaemia demarcation lines prior to visible changes ensuing. This may assist in defining the safe levels for bowel anastomosis and also demonstrate intestinal non-viability intraoperatively.

The effects of progressive compression by the AASP 2000 artificial anal Neosphincter were also studied in these patients. Progressive reduction of blood flow was observed with increasing inflation pressures. Colonic blood flow remained above 48% of its baseline value even at levels of system pressure beyond the sphincters' planned maximum settings. It appears that the Neosphincter is not likely to cause ischaemic injury to the human colon at the planned occlusion pressures.

A new control pump to operate the Neosphincter to overcome the problems associated with the existing device was specifically designed.

Further technological concepts may be incorporated to afford even more physiological features to the Neosphincter.

*I HAV FINALLY KUM TO THE
KONKLUSION, THAT A GOOD
RELIABLE SETT OV BOWELS IZ
WURTH MORE TO A MAN, THAN
ENNY QUANTITY OF BRAINS.*

Josh Billings (Henry Wheeler Shaw, 1818-1885)

His Sayings.

THE FUTURE

In this chapter, some thoughts will be presented on how to improve the AASP 2000 system based on original ideas, previous experience and also possibilities on the implementation of new technological concepts in the proposed designs.

Design of a new pump

The pump used for controlling the AASP 2000 (Figure 1) was based on the AMS 800 device.

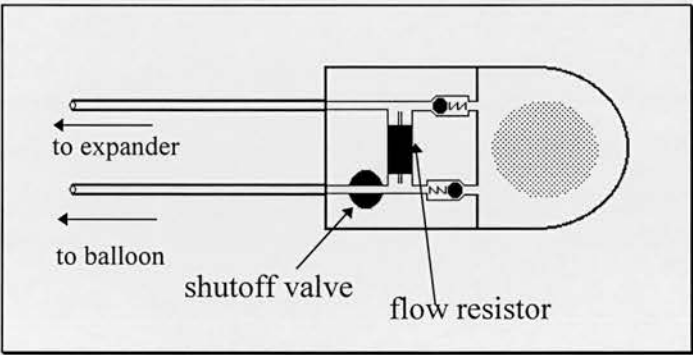


Figure 1: Schematic diagram of the control pump. The fluid flow restrictor (resistor) was made of a single narrow tube, whereas in the AMS 800 it was made of a porous glass material which was less susceptible to blockage.

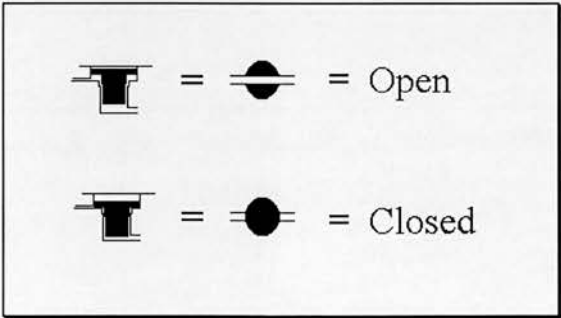


Figure 2: The shutoff valve. This simple “piston” type of valve was found to be unreliable.

Experience to date confirms the reliability problems of the shutoff valve (Figure 2), one way ball valves and the easily blocked resistor. The “piston” type valve was found to be unreliable (Chapter 3). AMS used a “waisted” design¹ for this component which conferred excellent reliability. The problems with the resistor were almost certainly due to the use of a single lumen narrow pathway resistor in the AASP design (Chapter 3) as opposed to a porous glass material with a high connectivity coefficient (Appendix 1) used by AMS^{1,2}. Other ergonomic and manufacturing details also need to be addressed. In addition, the design features suitable for controlling a urethral valve with automatic refilling/equilibration, although they make the device convenient and simple to operate by the patients, may not be ideal for controlling defæcation due to the long period the valve has to remain deactivated during defæcation.

One solution would be to develop the existing design further and manually shutting the shutoff valve at the initiation of defæcation and activating it on completion of evacuation. This would involve an extra **two** operations by the patient. This is not a major problem, however, as the current guidelines from AMS suggest that the device is maintained in its deactivated state during sleep. This would make the device identical to the commercially available unit with likely patent infringement^{1,2}. The necessity for a more controllable pump was recognized by AMS who, at the time, were exploring the control of urinary as well as fæcal incontinence. Their attempts to develop an alternative device were aborted in the early stages of its development³ in favour of the current AMS 800 pump.

In order to incorporate these design features, namely manually operated shunt pathway in place of the resistor in addition to a shutoff valve, I designed a new pump⁴ (Figure 3, Figure 4, Figure 5,). The shunting channel would be **de-activated by the first pumping stroke** of the bulb thus allowing the expander to be emptied and remain empty during defæcation. At the end of evacuation the **shunt is pressed** and returns to the "open" position thus allowing **fast equilibration** of pressure

rapidly closing the sphincter. This may be advantageous as slow equilibration may also allow time for stool to be interposed between the expander and the pillow thus leading to leakage. This design would entail **one** extra operation by the patient, that of pressing the shunt valve at the end of evacuation. The engineering implementation of the designs shown in Figure 3, Figure 4 and Figure 5 was difficult, and the prototype under development corresponds to Figure 6.

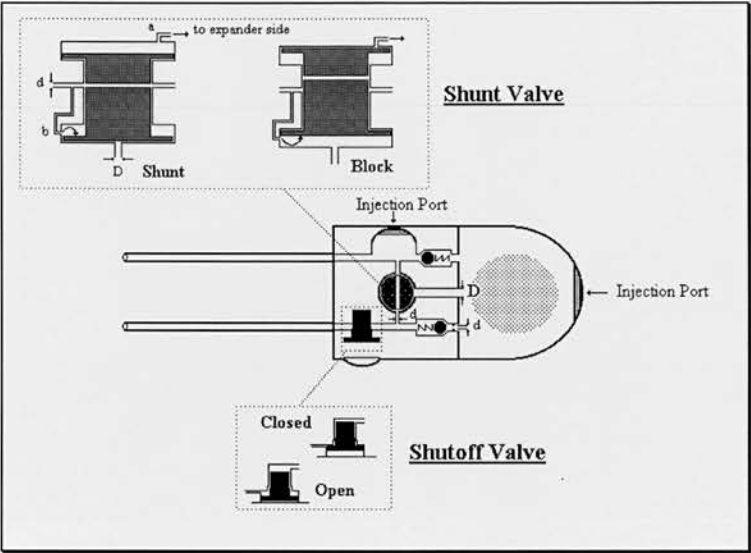


Figure 3: Proposed Pump for the control of faecal incontinence. Design incorporating Shunt Valve with pressure equilibrating channels, possibly providing a “stabilizing hydrostatic pressure” effect.

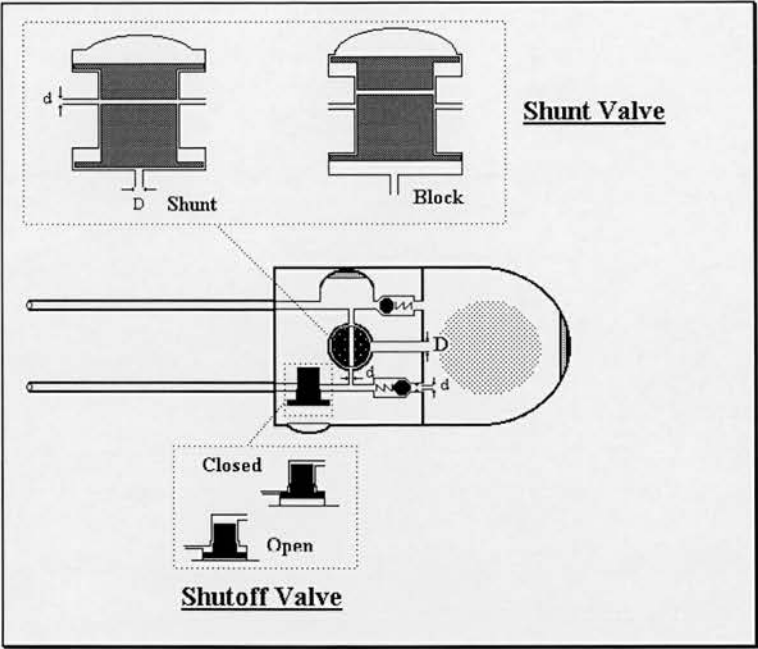


Figure 4: Proposed Pump for the control of faecal incontinence. Design with soft dome and without pressure equilibrating channels.

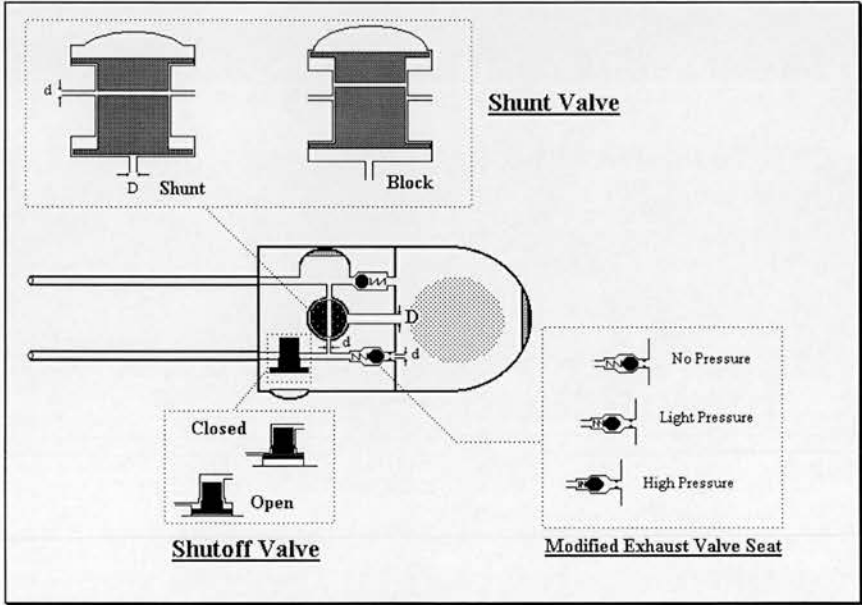


Figure 5: Proposed Pump for the control of faecal incontinence. Design with modified exhaust valve seat.

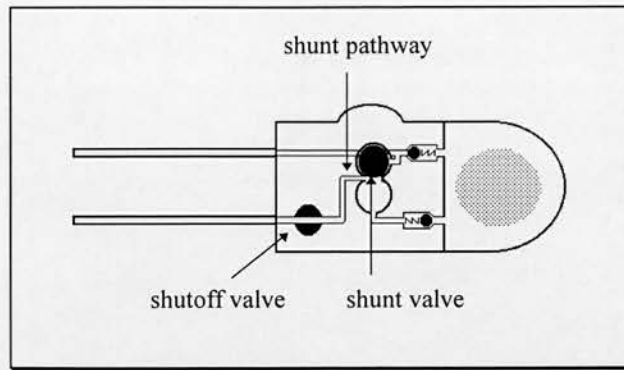


Figure 6: New control pump⁴ with manually controlled shunt pathway. The device is shown with the shutoff valve open and the shunt pathway blocked.

The shunt valve operation of the device is as follows: in the "block" position, the flow of fluid from the balloon to the expander side is checked. A pressure increase in the bulb is directly transmitted to the bottom of the shunt via channel D pushing it to the "shunt " position. The proposed designs in Figure 3 and Figure 4 depend on the faster transmission of the pressure wave through a wider channel (D)⁵ thus deactivating the shunt valve before this pressure wave is transmitted through the narrow channel (d) and dissipated through the shunt.

The device shown in Figure 3 depicts a design attempting to incorporate a "stabilizing pressure" applied to the shunt valve base through channel "b", akin to the current design in use where this pressure is applied on the top surface of the shutoff valve. Bench tests have proved that this does not confer any significant advantage to the reliability of the valve as the "unseating pressure" with a 100 mmHg pressure head is not significantly increased (Chapter 3). In addition, this channel has to be less than 0.2 mm in diameter, otherwise the balloon check valve would be rendered ineffective. In this design, channel "a" carries fluid to and from the expander side of the system thus allowing for the upwards or downwards movement of the shunt piston.

Figure 4 shows a design without channels "a" and "b". The former is replaced by the compliant dome which also allows for manual manipulation of the shunt, whereas the latter is not required.

Figure 5 introduces a modification in the valve seat of the balloon check valve: the valve is spring loaded and is normally closed as before, but by choosing a more compliant spring and introducing another valve seat on the exhaust side of the flow, the valve could allow fluid to be pumped normally by application of gentle slow squeezes on the bulb, whereas it would close and allow for shunt deactivation if the first stroke is sharp and quick. This design was considered to pose a very difficult task of manual dexterity both for the patient and the attending clinician and was not developed further.

Figure 6 and subsequent figures depict the theoretical operation of a design incorporating a **two compartment, three port poppet valve mechanism**, to achieve the desired shunting (see also Appendix 3). By placing this unit **in series** with the **shutoff valve**, the operation should become more reliable as the critical choice of the, now redundant, channels "d" and "D" is now obviated. The operation of the shutoff valve is depicted simply by an open or closed channel to aid clarity (Figure 2).

The operation would be quite simple: starting with a deactivated pump with a closed shutoff valve (Figure 7a), the patient would press the bulb, thus closing the expander side ball check valve and transferring the pressure wave to the bottom of the shunt ball or poppet valve (Figure 7b) and eventually "popping" the latter to the closed position (Figure 7c). This opens the shutoff valve during the same operation as the pressure is now transmitted to the bottom of its piston, and allows pumping to commence (Figure 7d).

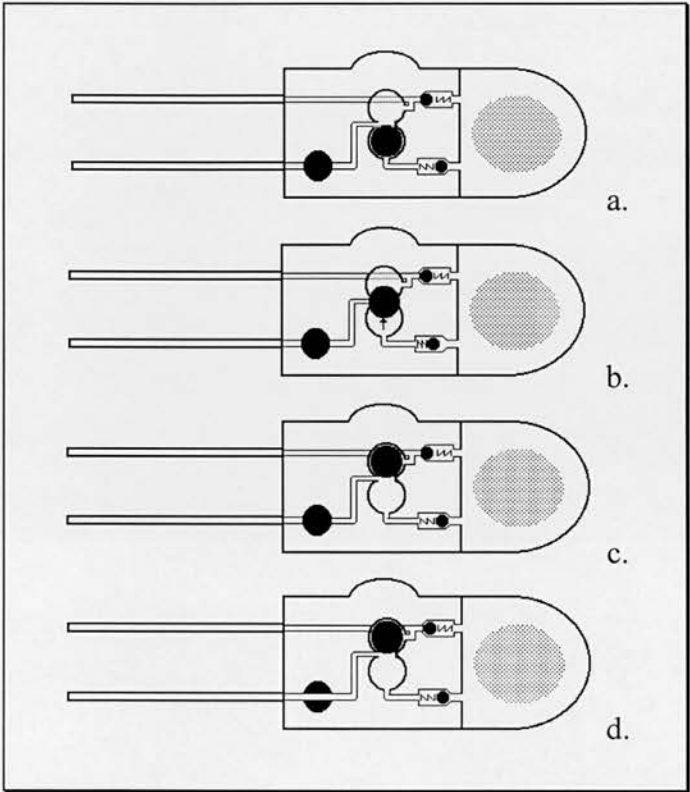


Figure 7: Manual operation of the new pump at the start of defæcation.

When the expander is emptied, evacuation commences and it remains empty until the patient has completed the act of defæcation (Figure 7d). The patient then presses the appropriate part of the case, which is easily deformed and identified by a bump, and this action pops the ball or poppet valve down to the "shunt" position and allows for rapid pressure equilibration and refilling of the expander (Figure 8a-d).

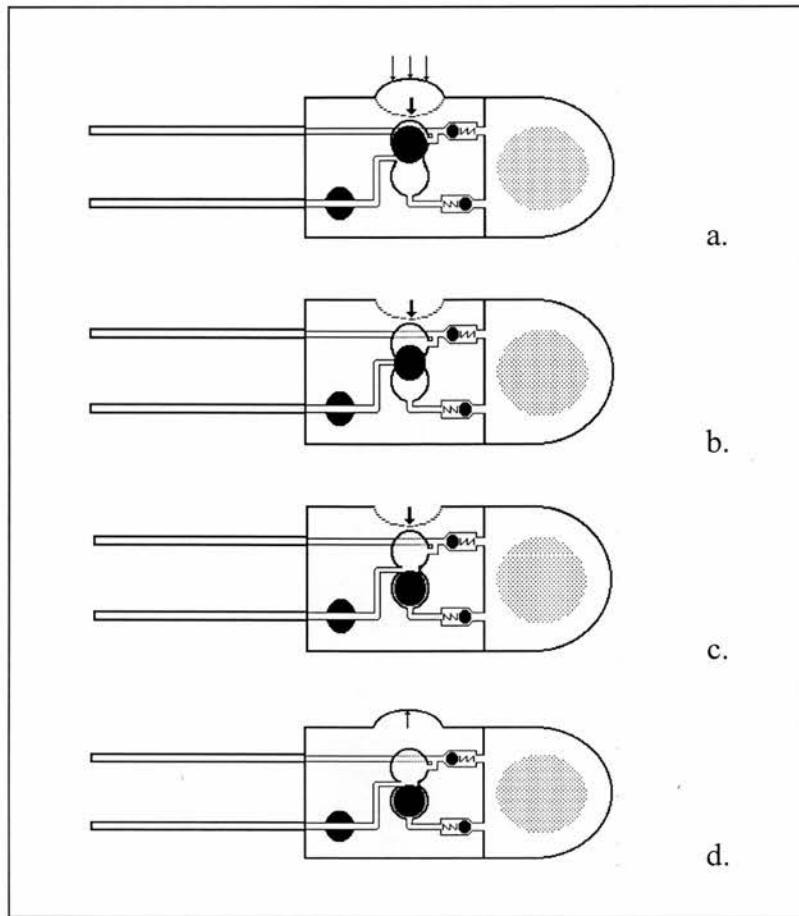


Figure 8: Manual activation of shunt valve.

In the above designs, the shutoff valve can be placed at 90° to the shunt valve, and this, in conjunction with a flat pump body design, would afford both space saving and ease of discrimination between the two valves. The presence of a separate shutoff valve is still desirable to ensure long term deactivation, e.g. during the suggested 3-6 week deactivation period postoperatively to allow for tissue healing⁶.

Programmable valve systems

These valves were designed and developed by Hakim and Hakim and patented by Codman-Medos⁷ (Figure 9, Figure 10). These valves were originally developed for the control of hydrocephalus shunting systems and are designed to precisely regulate the opening pressure of the system by external programming of a wireless servo motor.

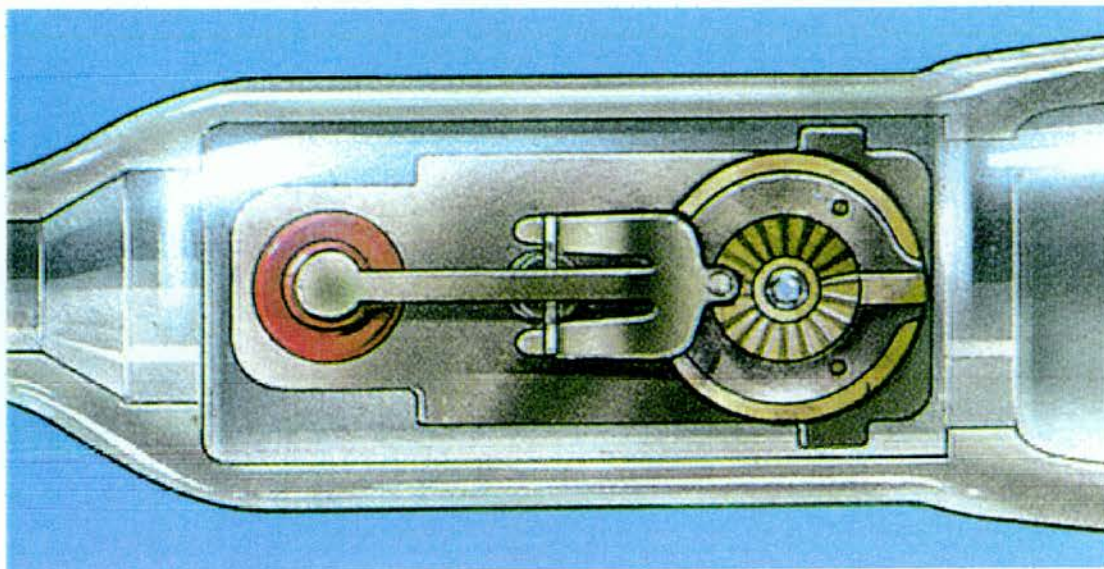


Figure 9: View of the Hakim valve from above.

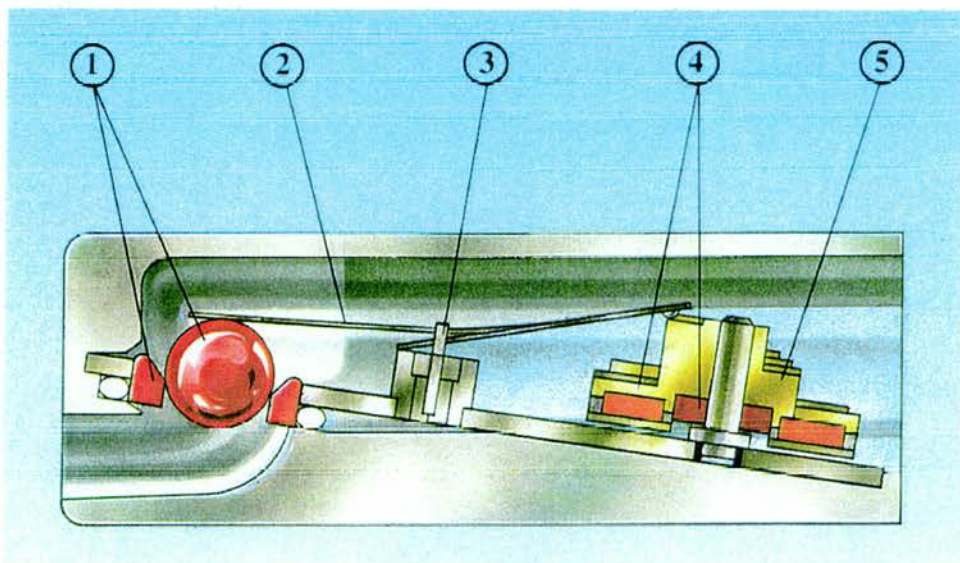


Figure 10: Cross section of the Hakim valve to show its components and operation (see text).

The ball valve and its seat Figure 10(1) are both made of synthetic ruby. Pressure is applied on the superior aspect of the ruby ball by a stainless steel spring element (2) the pressure characteristics of which are set by a telescopic fulcrum (3) and calibrated during manufacture. A wireless externally programmable stepper motor (4) incorporating a “spiral staircase” cam (5) on its superior aspect precisely sets the tension on the spring depending on the angle of rotation of the cam.

This design offers the possibility of multiple permutations and combinations that would be pertinent to an artificial sphincter control mechanism. The spring may be replaced by a rigid plate, which would transform the pressure control valve to an on/off switch. These could then be placed in series and/or in parallel with one another to replace the shutoff valve and possibly to also act as selector switches for the selection of one of several balloons (see next section: Balloon with multiple plateau pressures).

Balloon with multiple plateau pressures

One of the limitations of these designs is the inability to vary the operating pressure of the sphincter, unless a new balloon is inserted by revisional surgery. The animal experiments in this study were performed by setting the system pressure at a point along the slope of the sigmoidal pressure-volume curve, thus allowing for the option to inject fluid to raise the operating pressure if necessary. This, however, had the disadvantages of losing the protective effect of a pressure plateau and also meant that the operating pressure critically depended on a specific volume of fluid in the system.

One way round the problem, assuming a plateau is still considered necessary, would be to design a balloon with two or more plateaus so that pressure regulation could be effected over a certain range of inflation volumes which when exceeded would lead the system to a new higher plateau and so on. This idea is summarized in Figure 11 to Figure 13.

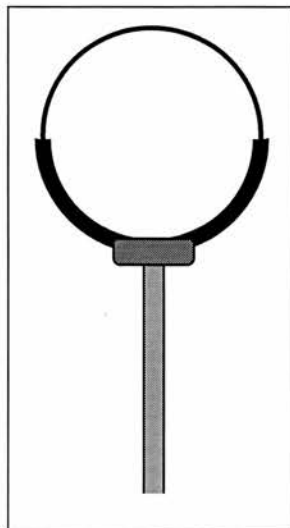


Figure 11: Proposed balloon made from two components of different pressure-volume characteristics to achieve a double plateau effect.

Figure 11 and Figure 12 depict the same proposed design, whereby two or more sections of the balloon are made of silicone of different thickness. The expansion of each segment could be limited over a specific range of the plateau for each one by internally placed expansion limiting elements (Figure 12). Upon progressive inflation, the pressure would increase almost in a stepwise fashion. Of course, the highest plateau should be set to a safe level which would not compromise tissue perfusion.

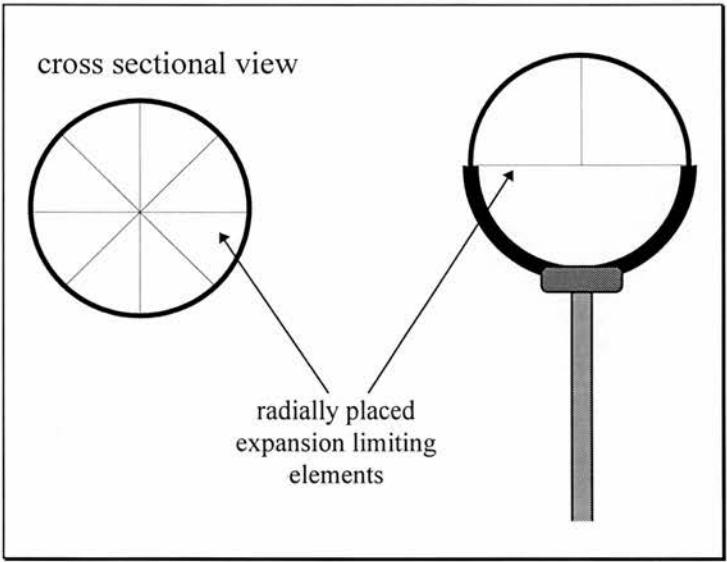


Figure 12: Same design as previous figure, but with the inclusion of balloon expansion limiting elements to set the range of volume for the pressure plateau during the manufacturing process.

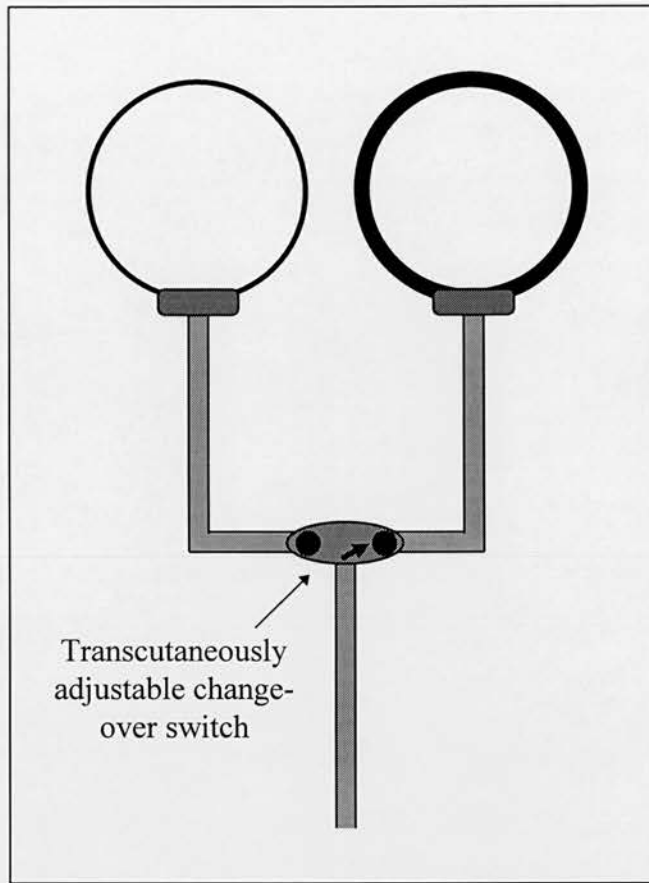


Figure 13: Multiple balloons with different plateaus could be connected together and each one selected by a change-over hydraulic switch.

Multiple balloons could be connected together and each one selected in a non-invasive manner if a reliable hydraulic switch was available (Figure 13). Magnetically operated valves were assessed by AMS⁸ but were not developed further.

An inductively activated and deactivated valve based on the shape memory effect⁹ would appear interesting. The basic mechanism governing the properties of shape memory alloys is a change in metal structure: a martensitic structure transforms, at a pre-defined temperature, into an austenitic structure during heating and reverts to the martensitic structure when the temperature is lowered again. Through careful processing, it is possible to associate a specific shape with each of the metal structures, and since structure is linked to temperature, this simply means

that a switch from low to high temperature or vice versa will result in a change in shape or, if this change in shape is prevented, in a force. The temperature range during which this transformation occurs is relatively small and can be freely chosen anywhere below 110°C. Such a biocompatible and corrosion resistant microactuator made from a Nickel-Titanium alloy (measuring 1.8X40 mm, weight 0.5 grams, activation time 0.1s, activation voltage 0.5-5V, load 1 Newton) is commercially available.

The design of a programmable switch around an inductively coupled stepper motor as described by Hakim⁷ should also be possible (see above).

Inductively coupled stimulation of the colon

Based on the current knowledge of faecal continence mechanisms which are reviewed in the first section, there is little doubt that an intact sensory pathway is essential for the maintenance of satisfactory control of defaecation. Simply inserting an artificial sphincter in a dysmotile colon would probably result in failure. The simplest option would be to condition the patient or “train” the colon to contract at a specific time each day, which would be convenient to the patient and deactivate the sphincter at that time.

Another possibility could involve the surgical insertion of a pair of stimulation electrodes into the bowel wall and stimulate these at will by inductive coupling. These electrodes could also be incorporated into the wall of the expander at the area of contact with the bowel during manufacture (Figure 14) and the inductive receiver would be placed subcutaneously. In a preliminary study using a signal generator (power 25 W, frequency 68 KHz), it was possible to induce a voltage of 3.5 V in an untuned coil (inductance 1 mH) placed 2 cm away. If this system is tuned and coded, then non-invasive colonic activation could be achieved and it should be possible to use different stimulating waveforms and stimulation modes as required.

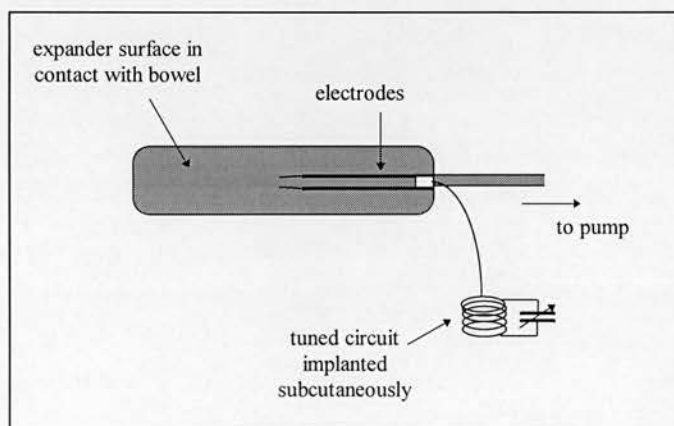


Figure 14: Proposed expander modification to incorporate a tuned receiver and stimulating electrodes to allow transcutaneous bowel stimulation.

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